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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

[*Continued from p.* 184.]

Treatment.

General.—In a comprehensive discussion of the principles governing the curative and suppressive treatments of malaria, especially in relation to military conditions, SINTON (p. 694) defines subdivisions of the terms prophylaxis, suppression and cure, and relates the procedures defined under these headings to the state of immunity of the troops (white and non-white) and to the malaria conditions to which they may be exposed. It is not possible further to condense this abstract; the author has taken into account all information available on the subject.

FINDLAY *et al.* (pp. 6, 350), in a study of the treatment of malaria in British troops in West Africa, all the infections being due to *P. falciparum*, conclude that mepacrine is as satisfactory as quinine, or as quinine followed by mepacrine, provided that 0·8 gm. is given in the first 24 hours of treatment. No toxic symptoms were seen, although some of the patients had been taking suppressive doses of mepacrine for several months beforehand. Quinine, however, should be used in cerebral malaria, hyperparasitism, in the rare cases in which the high temperature fails to react to mepacrine, and in the still more rare cases in which mepacrine causes vomiting or psychotic change.

In the *Army Medical Department Bulletin* (p. 692) it is stated that a quinine-pamaquin course was more successful than a mepacrine course in the treatment of relapses of *P. vivax* malaria. Subsequent relapses were significantly fewer after the quinine-pamaquin than after the mepacrine course during a follow-up period of 5 months. Details are given.

Evidence is brought by CHEN and GEILING (p. 348) to show that after intravenous injection, quinine and mepacrine are rapidly removed from the circulation by an adsorption process which takes place in the capillaries, especially those of the lung. Quinine is rapidly destroyed by enzyme action, but the metabolism of mepacrine in the tissues is slow, and the process is not yet understood.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

In March 1944 TEMKIN and RAMSEY (p. 533) issued a monograph on antimalarial drugs. This is a review of information published in the literature and was compiled as a basis for the revision which the military situation demanded, but it does not include the newly-acquired information then restricted to confidential reports, and may, therefore, be misleading to the student unless this is borne in mind.

Quinine, etc.—The effect of acid and alkali on the absorption and metabolism of quinine has been studied in animals by ANDREWS and CORNATZER (p. 534), who found that there was no evidence that alkali therapy significantly delayed excretion. The lowered percentage excretion of quinine during alkali administration, which has been noted by others, was confirmed, but the results are not explained by differences in absorption following administration of acid or alkali. The same authors have studied the rate and degree of absorption from the intestinal tract; the dihydrochloride is more quickly absorbed than the sulphate, but differences in the rates decrease with time.

PIRK and ENGELBERG (p. 964) show that administration of quinine has the effect of reducing the prothrombin level of the blood. Soldiers receiving it would therefore be in danger of prolonged bleeding, should they be wounded, and the authors advocate the concurrent administration of vitamin K in such circumstances.

HEILIG and VISVESWAR (p. 442) show that quinine, when given intravenously on several successive days, has a definitely deleterious action on the myocardium, and leads to lowering of the blood pressure, probably through an action on the peripheral vessels. They conclude that quinine should not be given intravenously unless there is a specific indication. DREISBACH and HANZLIK (p. 964) agree that quinine given intravenously has a depressant action on the circulation which, in cases of severe quinine collapse, may be irreversible; they have found that epinephrine, neosynephrine and calcium chloride, when mixed with the quinine, have an action in mitigating this depressant action. Details of dosage are given.

KHAN (p. 861), as a result of a considerable experience in a military hospital, states that a not inconsiderable proportion of blood slides of patients seriously ill from malaria were repeatedly negative for parasites, and that in some fatal cases where this was so, sporulating forms were found in the capillaries of the brain post mortem. In the majority of serious cases, however, the blood was heavily infected. In suspected cases of cerebral malaria, intravenous quinine should be given immediately, but for further treatment the author favours intramuscular methyl-sulphonate-mepacrine. For cerebral malaria FITZ-HUGH *et al.* (p. 340) gave intravenous injections of quinine, well diluted in saline or saline-glucose, and administered slowly. As much as 3 or 4 gm. quinine may be given in 24 hours. Intravenous sodium amytal is most useful in convulsions or mania, and spinal drainage in coma. Blood or plasma transfusions are valuable for anaemia or symptoms of shock.

METCALF and UNGAR (p. 341) describe patients with *P. vivax* malaria, contracted in the Solomons, who had to be repatriated to the United States because of relapses. These men were unable to achieve immunity strong enough to permit them to remain abroad, and treatment with mepacrine was not efficacious. The drug of choice was quinine in heavy dosage; there was little advantage in using mepacrine, pamaquin or neoarsphenamine with the quinine. In these men a low degree of parasitaemia was capable of producing a severe rigor.

For the treatment of relapses of *P. vivax* malaria, in men returned to Britain from abroad, MANSON-BAHR (p. 176) advocates the use of Solvochin, a preparation of quinine for intramuscular injection, the dose of which contains 0·5 gm. quinine. The injections (two daily for two days) should be followed

by a course of quinine by the mouth, and of pamaquin. For *P. falciparum* infections more injections may be needed, followed by oral quinine and mepacrine. Solvochin contains antipyrin. HAWKING (p. 536) has shown that the lesions it causes in muscle are indistinguishable from those caused by quinine. BROWN (p. 779) has found X-ray evidence of calcified "cysts" in the gluteal region of European and Indian soldiers who have received intramuscular injections of quinine. Their appearance is characteristic, but they give no trouble.

RAYMOND (p. 250) shows that the totaquina (type I) prepared in Tanganyika Territory contains all the cinchona alkaloids and, though in somewhat larger dosage, is practically as useful in treatment as quinine. He argues that totaquina of this type is the most economical and effective means of using the anti-malarial action of cinchona bark. A comment in the *East African Medical Journal* strongly supports this view (which, indeed, is widely held) and urges standardization of totaquina. A controlled experiment carried out by GREEN (p. 442) shows that treatment of malaria (chiefly *P. vivax* infections) with totaquina was about as effective as treatment with quinine, but that mepacrine was more successful in preventing early relapses than either totaquina or quinine.

RICO (p. 177) reports favourably on a gluconate of quinine and calcium in treatment.

The distribution of quinine and other cinchona alkaloids in the fluids and tissues of dogs has been studied by HIATT and QUINN (p. 778); for details the original abstract should be consulted. UNTI (pp. 90, 697) describes a simple method for the estimation of quinine in blood. HIATT (p. 178) has determined the plasma concentration of alkaloids of cinchona, at various times after a single oral administration.

MEAD and KOEPFLI (p. 9) discuss the structure of a quinine derivative obtained by allowing rabbit liver to react with quinine *in vitro*.

DAVIDSON (p. 964) has found that burasaine (a mixture of alkaloids) has some definite antimalarial properties.

Mepacrine.—In 1944 the Medical Research Council Committee on Malaria (p. 88) issued a statement on mepacrine, in which they reproduced a resolution made by the United States Board for the Co-ordination of Malarial Studies. There was very close agreement between the opinions expressed, which may be summed up as follows. Under proper administration mepacrine is no more liable than quinine to cause toxic effects; mepacrine is as effective as quinine in the treatment of *vivax* malaria, but neither compound will prevent relapses; if properly given, mepacrine will practically always suppress and cure *falciparum* malaria, but the action of quinine in this respect is less certain. The Americans point out that mepacrine is effective in suppression [they do not distinguish species in this respect] and that doses of quinine sufficient to produce the same result frequently cause symptoms of cinchonism.

In an important paper on the pharmacological basis of mepacrine therapy in malaria, SHANNON *et al.* (p. 343) show that the concentration of this drug in leucocytes is more than 200 times as great as the concentration in plasma, and that the ratio between the concentrations in whole blood and plasma varies considerably, for a number of reasons. When blood is shed, the mepacrine tends to be released from the leucocytes, and it is therefore important that the blood should be centrifuged immediately after withdrawal, if the plasma estimations are not to be vitiated. Most of the mepacrine in plasma is bound to the proteins. In the different organs of the body the concentration of mepacrine varies greatly, being highest in the liver, and only relatively small fractions are retained in the plasma. Excretion of mepacrine is slow and accounts for only 1–5 per cent. of the daily dose; degradation is also

slow, and mepacrine can therefore accumulate in the body to reach a point of equilibrium which varies in different individuals. Protection against malaria, as noted by HAWKING in comment, is probably achieved at a plasma concentration of about 20 microgm. per litre, and this is attained most quickly by high initial dosage. Similarly, for treatment, a high initial dosage should be used; for this mepacrine may be injected intramuscularly, but the intravenous route is not advised. Subsequently it should be given by mouth. Details will be found in the original abstract.

MASEN (p. 8) describes a method for the fluorimetric estimation of mepacrine in blood and urine, which is sensitive to 0·1 mgm. per litre. Details should be sought in the original. AUERBACH and ECKERT (p. 90) have used a modification of this method, which is described.

MAEGRAITH *et al.* (p. 251) have shown that the concentration of urinary mepacrine is proportional to that of plasma mepacrine and to that of urinary ammonia, so that if any two of these values are known, the third can be calculated by means of a simple formula. Plasma concentration, which is a most important factor, is difficult to determine, but urinary mepacrine and ammonia concentrations can be estimated simply by means of a Lovibond disk. KING and GILCHRIST (p. 781) describe a method for estimating mepacrine in urine, for details of which the original abstract should be consulted, and BROWN and RENNIE (p. 780) and MAEGRAITH *et al.* (p. 780) have observed that, in persons who have been taking suppressive mepacrine for some weeks, the plasma mepacrine can be calculated from a formula which takes into account urinary mepacrine, urinary NH_3, and a constant. The latter workers (p. 779) show that the error in this procedure is very small, and that the apparatus is simple. The method can be adapted to régimes of mepacrine administration other than suppressive doses, but for each régime special measurements are necessary.

YUDKIN (p. 863) describes three simple methods for the estimation of mepacrine in urine, for details of which the original abstract should be consulted.

KING and GILCHRIST (p. 782) describe a field method for the estimation of mepacrine in plasma and blood; details cannot be given in brief space. The method depends on fluorescence, as does that described by HENRY and GRINDLEY (p. 783) for estimation of stilbamidine and mepacrine in urine.

A paper was published in the *Lancet* (p. 342) by the Army Malaria Research Unit, which showed that in estimation of plasma mepacrine the anticoagulant used should not contain ammonia, since ammonia displaces mepacrine from the leucocytes (which have a high concentration of the drug), and therefore leads to grossly exaggerated plasma readings. Potassium oxalate, sodium citrate and heparin are satisfactory anticoagulants.

LEWIS (p. 443) describes a method, details of which are given in the original abstract, for estimating concentrations of mepacrine in serum. In comment, HAWKING points out that since vastly larger amounts of mepacrine are held in leucocytes than in plasma, the separation of serum introduces the probability of error by liberation of mepacrine from the white cells. The ideal is to estimate mepacrine in plasma separated from cells within 15 minutes of withdrawal from the body; if this cannot be done, mepacrine should be estimated in whole blood, a leucocyte count being made so as to guard against gross abnormalities.

ALLEN (253) points out that patients who have taken large doses of mepacrine may develop a mental condition similar to that of general paralysis, and that a false positive Wassermann reaction may be found, in such cases, as a result of malaria. The results that may follow such a mistaken diagnosis are obvious. GASKILL and FITZ-HUGH (p. 629) report toxic psychosis in 0·4 per cent. of soldiers suffering from malaria and treated with mepacrine; most

of these patients recovered. GELLER (p. 9) has not found that relatively large doses of mepacrine produce nervous symptoms. In comment, HAWKING states that psychotic symptoms due to mepacrine have occurred but rarely in the wide experience gained in the recent war, and that such symptoms usually disappear when the mepacrine is discontinued.

In *Nutrition Reviews* (p. 8) a summary is made of the evidence which shows that mepacrine, in high dosage, may have a toxic action in animals poorly nourished, especially in regard to proteins.

SIEGEL and MUSHETT (p. 178) give an account of the pathological changes induced in animals by administration of large doses of mepacrine. For details the original abstract should be consulted. SIEGEL *et al.* (p. 628) show that very large doses of mepacrine given to rats on a low-protein diet caused damage to the liver, but, in comment, HAWKING points out that in man the ordinary suppressive dose does not produce any visceral lesions. In men treated for malaria with courses of mepacrine in fairly high dosage, BUTT *et al.* (p. 783) could find no evidence of damage to the liver, a conclusion which agrees with that of military investigators in the British Army.

In experiments with young rats, HEGSTED *et al.* (p. 784) have found that mepacrine has a thiamin-sparing action.

THOMPSON (p. 695) has treated relapses of *P. vivax* malaria with large initial doses of mepacrine, with some apparent benefit over courses comprising smaller doses. SMITH and PASSALACQUA (p. 696) also write favourably of the effects of large doses of mepacrine, especially in *P. vivax* malaria.

The pharmacological action, especially as regards toxicity, of eight salts of mepacrine was studied in animals by BARLOW *et al.* (p. 443). Details should be sought in the original.

BOSE *et al.* (p. 444) show that a butyl acridine derivative (the corresponding amyl acridine compound being mepacrine) has considerable effect in *P. vivax* and *P. falciparum* infections.

Pamaquin, etc.—WEST and HENDERSON (p. 253) give a list of symptoms which they attribute to the use of pamaquin (plasmoquine) in doses of 0·01 gm. daily for 5 days in American troops overseas. These symptoms include jaundice, abdominal pain, anaemia, headache, weakness and dizziness. In comment, HAWKING observes that it is difficult to exclude other factors as causes of this syndrome, and points out that no such complaints were made in a considerable group of British soldiers treated in much the same way.

SHISHLAEVA-MATOVA (p. 351) produces evidence that the compound "Quinoline No. 31" [the chemical name of which is given in the abstract] is about as effective as pamaquin in preventing infection of mosquitoes with both benign and malignant tertian parasites.

Other Drugs.—COGGESHALL *et al.* (p. 698) have shown that sulphadiazine has no value in preventing relapses in *P. vivax* malaria naturally acquired in the South-West Pacific.

HARNED and ETTELDORF (p. 443) show that sulphathiazole can be administered concurrently with quinine or mepacrine. In malarious districts such a combination is necessary when bacterial diseases and malaria co-exist.

KAY (p. 696) found no advantage from giving three injections of Mapharsen in conjunction with mepacrine in the treatment of relapsing *P. vivax* infections. On the other hand DAO (p. 697) reports good results from the use of this drug alone in *P. vivax* infections, injections being given at intervals of 4 to 7 days for courses of eight injections.

HINDLE *et al.* (p. 446) have found that penicillin is without effect in malaria.

Suppression.

FINDLAY and STEVENSON (p. 349) recount the history of drug suppression of malaria in West Africa during the war. Quinine in 5–10 grain doses was not satisfactory, mepacrine (0·4 gm. each week) was better, but the best results were obtained with mepacrine 0·1 gm. daily except on Sundays. Figures are given which demonstrate these facts beyond doubt. The only cases of cerebral malaria were in men who either had not taken mepacrine or had taken it irregularly. The use of mepacrine appeared to reduce the number of cases of blackwater fever. [The findings in West Africa are therefore in line with those of workers in New Guinea.]

FAIRLEY (p. 656) comments on the high rate of malaria experienced by the troops in New Guinea before the use of suppressive mepacrine became universal. To test the suppressive and therapeutic effectiveness of mepacrine, quinine and certain sulphonamides, FAIRLEY (p. 630) and his associates made very careful investigations on healthy volunteers in Australia. These men were infected with Papuan strains of *P. falciparum* or *P. vivax*, and were subjected to most rigorous conditions. The author makes the point that no instance was seen of failure to infect the normal white man unless he was protected by a drug. The sulphonamides suppress *P. falciparum* but not *P. vivax*; mepacrine in a daily dose of 0·1 gm. suppresses and will cure *P. falciparum* infection if continued for some weeks after exposure, but though it suppresses it, it will not usually cure *P. vivax* infection. Quinine is not nearly so effective. Institution of suppressive mepacrine as a routine, and made a disciplinary measure, in the troops in New Guinea brought about a most dramatic reduction in the incidence of malaria, but the problem of relapses of *P. vivax* after cessation of mepacrine administration remains. In this work it is shown that though blood is infective for a few minutes after infection by bite, it becomes uninfective until the 7th (*P. falciparum*) or 9th (*P. vivax*) day; sporozoites are apparently rapidly removed by macrophages and fixed tissue cells.

In the *Royal Naval Medical Bulletin* (p. 179), recommendations made in the United States Navy for the use of mepacrine as a suppressive are reproduced. These follow the accepted dosage of 0·1 gm. daily, and the point is made that the treatment should be commenced a month or more before arrival in the malarious area, or that if time is short, 0·2 gm. daily for a week should be taken to build up the necessary blood concentration.

MCCOY (p. 785) sums up the use of mepacrine, for suppression of malaria, in doses of 0·1 gm. daily. Symptoms of intolerance usually pass off quickly. They very rarely persist. It is necessary to attain the required plasma concentration by administration for some time before exposure to malaria, and it may be necessary, in military operations, to continue administration for some time after cessation of exposure. There is no evidence of the production of mepacrine-resistant strains of parasites as a result of long-continued administration.

From investigations in Lebanon, MEASHAM *et al.* (p. 695) conclude that mepacrine, though not a true prophylactic, is a useful suppressant, and that if continued long enough, it cures infections at a subclinical level.

Suppressive treatment with mepacrine and pamaquin given on two successive days every 5 days was found by LEITMAN (p. 254) to be useful in the prevention of malaria in Tashkent. In a comparison of the effects of mepacrine alone and of mepacrine together with pamaquin, in adult doses of 0·3 gm. and 0·03 gm. of the two substances weekly, scaled down for younger persons, PARROT *et al.* (p. 445) found that neither was effective in preventing malaria in the inhabitants of a hyperendemic area of Algeria.

MAEGRAITH and HAVARD (p. 863) made long and detailed studies on some 500 volunteers in relation to the effects of mepacrine taken in suppressive doses. They concluded that the drug is both safe and effective. As a result of careful examination of 102 soldiers, DREW and REID (p. 862) think that prolonged administration of mepacrine in suppressive doses does not lead to any cumulative toxic action, and that there is good reason to believe that its protective action is very great. MCCORKLE (p. 536) concludes from an investigation that prolonged administration of mepacrine in suppressive doses has no deleterious action on the liver, and in comment HAWKING states that elaborate investigations in Britain have led to the same opinion.

RUSSELL (p. 630) produces evidence which suggests that mepacrine in suppressive doses tends to produce some degree of eosinophilia.

ROMERO MOLINER (p. 180) shows that in Fernando Po a daily dose of 0·4 gm. quinine was not an effective suppressive. Atepe (containing mepacrine and pamaquin) was much more successful.

Control.

In an address on the need for a malaria control policy for rural Africa, MACDONALD (p. 965) claims that in spite of the relative immunity attained by Africans after the age of childhood, malaria still continues to be a cause of ill-health in adult life, and he is not content with the view that it is unwise to attempt malaria control because anything less than complete control would interfere with immunity. He advocates experiments on a large scale, in which all the methods now available should be used, together with improvement of the whole circumstances of African life. ANNECKE *et al.* (p. 966), on the other hand, restate the argument that incomplete control would make matters worse in the hyperendemic areas. They see more hope from improvement of environmental conditions and nutrition, so that the Africans may be more able to resist malaria, than from control by methods now used. They, too, advocate continued research and experiment on a large scale, but think that the means of control now available are not likely to give satisfactory results in the areas concerned and under existing conditions. A single and cheap form of attack is required.

SYMES and HADAWAY (p. 785) have made a detailed investigation of the effect of DDT, in solution or as an emulsion, in killing adult mosquitoes in dwellings in British Guiana. The results were very good, and the residual action most notable—in one area the reduction of anophelines (compared with control houses) was 95·9 per cent. 7 weeks after application. *Anopheles darlingi* is more susceptible than *Culex fatigans* to DDT. Discharge into the open air is also effective, but needs investigation. The authors note that, in the daytime, *A. darlingi* frequents ground shaded by vegetation, and that ground-spraying is therefore essential.

RICE *et al.* (p. 632) show that Thanite, a terpene thiocyano ester, incorporated in DDT sprays, greatly increases the immediate knock-down effect; the residual lethal action, however, is due to DDT.

EDDEY (p. 255) describes the programme of spray-killing of adult mosquitoes (chiefly *A. gambiae*) which was undertaken in Takoradi during the war. The best results were obtained with pyrethrum aerosol and pyrethrum in kerosene [DDT evidently not being available]. The procedure was popular, and malaria rates are quoted which suggest that there was a substantial reduction of incidence as a result of this measure.

Dusting of African huts with pyrethrum powder at the rate of 2 ounces per 1,000 cubic feet, twice each week, was found by GARNHAM and HARPER (p. 447) to reduce by about 50 per cent. the amount of malaria in a village in Kenya at an altitude of 5,000 ft., in which transmission was largely seasonal.

Senior WHITE and VENKAT RAO (p. 180) have made an extensive study of the daily movements of *Anopheles* of the *fluviatilis* group (*fluviatilis*, *minimus* and *varuna*) in relation to houses baited with man or animals, and of the effects of spraying (at various intervals) on the older (and potentially infective) mosquitoes. The rationale of spraying is to destroy the mosquito before it becomes infective, *i.e.* before the 9th–14th day, according to the time of the year. The authors therefore suggest that spraying should be spaced so that any mosquito will twice run the risk of being hit before its glands become infected. By daily spraying the density of mosquitoes was (in one experiment) reduced 24-fold; by intermittent spraying, with intervals of not more than 2 days, 6-fold. The oöcyst and sporozoite rates of the mosquitoes caught did not vary much, but it is by the reduction of density that malaria control is achieved. *A. culicifacies*, however, can be controlled by weekly, or at most twice weekly, spraying. For details the original abstract should be consulted.

GILROY and CHWATT (p. 786) describe their method of draining that part of the foreshore near Lagos, which is covered by the sea only by high tides, and in which there are many crab holes and shallow pools. This zone is the chief breeding place of *A. melas*. By constructing an embankment on the seaward side of this zone, and draining the zone by one-way gates through the embankment, the authors effected a marked fall in anophelines over a large area; the malaria rate also fell, but there may have been additional reasons for this, notably the removal of the local population of gametocyte carriers.

COLLIGNON (p. 698) reports on anti-malarial measures taken in the Department of Algiers during 1943.

Emulsions of mineral oils have successfully been used in larval control by KANCHAVELI (p. 632).

WASICKY and UNTI (p. 182) have tested DDT, in a colloidal preparation, as a larvicide. A dilution of 1 in 50 million kills mosquito larvae in 24–36 hours and there is a residual action, in gradually diminishing potency, for several weeks.

ROZEBOOM and HESS (p. 182) show that there is a close positive correlation between the production of *A. quadrimaculatus* and the extent of intersection line between plants, water and air. High intersection line values conduce to increased oviposition and decreased larval mortality. HESS and KIKER (p. 183) describe the means by which the breeding of *A. quadrimaculatus* is controlled on the great reservoirs of the Tennessee Valley Authority. By bringing the water level to full during winter or spring, and then reducing to summer level, much of the floatage is stranded and rendered harmless. Later, a constant level reduces the amount of subsequent marginal vegetation, but from the beginning of moderate *quadrimaculatus* production, weekly fluctuation of level eliminates the intersection line and produces a clean shoreline. The permanent works undertaken for the control of *Anopheles* breeding on the Kentucky reservoir of the Tennessee Valley scheme are described by BISHOP and GARTRELL (p. 184) who show that in projects of this kind such works are more economical than the larvicidal and shore line maintenance programme which would have been necessary had they not been done. Details must be sought in the original.

A description of technical methods in the use of aeroplanes for dusting with Paris green is given by KRUSE *et al.* (p. 184). This method of mosquito control is largely used in the Tennessee valley. METCALF and HESS (p. 351) note that when Paris green is used from aircraft, only about 25 per cent. reaches the treatment area, the rest being dispersed by wind and propeller action. They found that if particles of larger size (20–50 microns) than usual are employed, there is a 60 per cent. increase in the amount which reaches the treatment area, and that particles of these sizes are, in fact, ingested by larvae of *A. quadrimaculatus*. They therefore recommend the use of larger particles.

Schoof (p. 537) shows that non-baited anopheline houses—rough wooden structures easily made and transported—afford the most useful means of observing adult *A. quadrimaculatus* in relation to control measures.

Mulrennan *et al.* (p. 633) quote instances of potential malaria vectors from foreign countries being found in the United States, and comment on the need for strict supervision of aircraft which may bring such dangerous species.

Malaria of Birds and Monkeys.

Brooke (p. 864) gave to canaries diets in which there were certain deficiencies comparable with deficiencies in human diets in parts of the United States and elsewhere. He observed the effect of these diets on the course of infection with certain bird malaria parasites; in general this was to cause the birds to suffer from more severe primary attacks, and to reveal a greater tendency to relapse and a reduced resistance to superinfection. Biotin deficiency increases the severity of certain avian malarial infections, but Seeler and Ott (p. 540) produce evidence that riboflavin deficiency has rather the opposite effect.

Seeler (p. 699) has found that administration of pyridoxine definitely inhibits the action of quinine and mepacrine in certain malaria infections of ducklings, but does not influence their toxicity. It is not known how pyridoxine acts in this respect.

Wright and Sabine (p. 252) discuss the effect of mepacrine on the oxygen consumption of tissues, and Haas (p. 252) has investigated the effect of mepacrine and quinine on isolated respiratory enzymes. Readers are referred to the original abstracts for the results of these highly technical studies.

Speck and Evans (p. 967) have shown that *P. gallinaceum*, like *P. knowlesi*, forms lactic acid from glucose. They discuss the action of quinine and mepacrine on the metabolic activities of *P. gallinaceum* in relation to therapeutic activity. Silverman *et al.* (p. 448) have studied the metabolism of *P. gallinaceum in vitro*, but for details of this intricate work the reader should consult the original abstract.

A comprehensive description is given by Huff and Coulston (p. 538) of the development in chickens of *P. gallinaceum* from sporozoite to erythrocytic trophozoite. The sporozoite, whether injected by syringe or mosquito bite, develops in macrophages, divides into cryptozoic merozoites, which in turn give rise to metacryptozoic merozoites which enter either other macrophages, or erythrocytes. A later stage of development consists of the formation of larger numbers of small (micro-) merozoites, and at this stage there is a sudden flooding of the blood with erythrocytic forms. The only species of malaria parasites in which cryptozoites have been found are those in which abundant exoerythrocytic stages occur; it should not be assumed that all species of *Plasmodium* must develop in the same way. This description of the development of *P. gallinaceum* is the first complete account which has been given.

Cantrell and Jordan (p. 633) have found all species of *Aëdes* tested to be susceptible to *P. gallinaceum* infection. *Culex pipiens* is resistant.

Haas and Ewing (p. 539) have succeeded in infecting chick embryos with *P. gallinaceum* by inducing infected mosquitoes to feed through the shell membrane. Haas *et al.* (p. 865) have devised a technique for making serial passages of *P. gallinaceum* in chick embryos. They note that a green discoloration of the membranes, amniotic fluid, yolk, liver and spleen is diagnostic of malarial infection.

Coatney *et al.* (p. 865) discuss the results of experiments on infection of chicks with *P. gallinaceum* either by the bite of a single infected *Aëdes aegypti* or by injections of sporozoites or of comminuted whole mosquitoes. The last is the method of choice for inducing infection for studies in chemotherapy.

COGGESHALL *et al.* (p. 699) have devised a method of obtaining brain material from chickens, for the study of exo-erythrocytic forms of *P. gallinaceum*, without causing much damage to the birds. They have tested the effect of various drugs on these parasites, and find that sulphadiazine and sulphapyridine [? sulphapyrazine] have an action, but that quinine and mepacrine have not. Though sulphadiazine and sulphapyrazine are able to eradicate exo-erythrocytic forms of *P. gallinaceum*, THOMPSON (p. 787) found that they had no such action on these forms of *P. elongatum*, which develop in various blood- and blood-forming cells.

Experiments in birds have shown that both sulphadiazine and sulphaguanidine exert a definite prophylactic action against infection with *P. gallinaceum*, but the dosage used by COATNEY and COOPER (p. 353) was higher than that normally employed in human therapeutic experiments. Sulphaguanidine was less effective than sulphadiazine.

Tyrothricin has a definite action against *P. gallinaceum* in chickens, but TALIAFERRO *et al.* (p. 449) show that it is useful only when given intravenously, and that it is much more toxic than quinine, with which it is compared. The effect of tyrothricin is predominantly parasiticidal on extracellular merozoites, whereas quinine chiefly inhibits reproduction. The markedly curative and suppressive activity of tyrothricin is paralleled by that of gramicidin, a product separated from tyrothricin.

Sodium iodobismuthate has some antimalarial action in *P. gallinaceum* infections of chicks (GUERRA *et al.*, p. 866).

GAJEWSKI and TATUM (p. 92) have made a careful study of the mechanism of relapse in avian malaria. They exposed canaries which had latent infections with *P. cathemerium* to atmospheres in which the oxygen pressure was reduced. This brought about relapse, and was accompanied by increased production of young erythrocytes which, as is known, are preferred by merozoites of some avian malaria parasites. There is evidence which suggests that low oxygen pressure in some way interferes with phagocytosis. Low oxygen pressure also produces hyperglycaemia, and the authors found that hyperglycaemia produced by other means also produces similar results. There seems to be some substance formed as a result of malarial infection, which sensitizes the phagocytes to remove the parasites from the peripheral blood, and at low oxygen pressure, or in hyperglycaemia, the formation of this substance is to some extent suppressed, though if the oxygen pressure is maintained at a low level this phase passes off and parasites are again reduced.

CALDWELL (p. 94) has shown that exposure of certain strains of *P. cathemerium* to a temperature of 50°C. for 7 minutes (just below the lethal exposure) in some cases resulted in infections, in subsequently inoculated birds, which had lost the regular features characteristic of the original infection. This, however, did not always happen, and if it did, the change was not always persistent.

STAUBER and VAN DYKE (p. 540) show that the duck embryo can be infected with *P. cathemerium* or *P. lophurae*.

In experiments on the simultaneous infection of ducks with approximately equal numbers of blood forms of *P. cathemerium* and *P. lophurae*, WOLFSON (p. 867) found that each infection followed its course as if the other was not present.

Observations on the mosquito transmission of *P. lophurae* are recorded by JEFFERY (p. 352).

The pathology of *P. lophurae* infection of the duck is described by RIGDON (p. 540).

REDMOND (p. 95) quotes evidence which suggests that passage through *Culex pipiens* produced genetic changes in a strain of *P. relictum*.

Tze-Tuan Chen (p. 185) records the results of his study of the nucleus of *P. elongatum*.

Simpson (p. 10) has found exo-erythrocytic schizonts of *P. durae* in turkeys.

Bose & Rakshit (p. 451) have estimated the action of certain substituted quinoline and acridine compounds on the gametocytes of *Haemoproteus columbae*. One of these [which appears to be the same as Quinoline No. 31, see Shishlaeva-Matova, above] was effective, though relapses occurred. For details of the others the original abstract should be consulted.

Ball *et al.* (p. 867) have succeeded in cultivating *P. knowlesi* in blood diluted with a complex nutrient fluid, or separated from it by a membrane. After 6 days' growth the parasites were still able to infect. By this means the metabolism of the parasites may be susceptible of study.

Dulaney and Morrison (p. 352) find that phosphate or barbiturate buffer extracts of *P. knowlesi* are better than saline extracts for use in the complement fixation test for malaria. These can be dried and stored without loss of potency.

Patel (p. 448) has shown that certain thiazole derivatives of sulphanilamide are effective in *P. knowlesi* infections of monkeys. Das Gupta and Siddons (p. 537) have found stilbamidine useful in the treatment of *P. knowlesi* infections in monkeys.

Taliaferro and Taliaferro (p. 256) have studied the effect of immunity on the asexual reproduction of *Plasmodium brasilianum* in monkeys. It seems that natural immunity functions alone during the acute rise in the infection, but is reinforced by acquired immunity at the time of the crisis. Each form causes death of the parasites and reduction in the rate of asexual reproduction. These changes are regarded as due to the effect of parasiticidal antibodies, though changes in the host as a result of the intense antigen-antibody reaction at the time of the crisis may also, to some extent, be responsible.

Thompson (p. 541) gives a description of the malaria of lizards.

Charles Wilcocks.

MALARIA.

Smith, R. L. **Significance of Palpable Spleens in Malarious Areas of Low Endemicity.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 155–64. [14 refs.]

In order to appraise the value of the spleen index as a measure of malaria endemicity in areas of low malaria prevalence, examinations were made of a group of children in a known non-malarious area and a group of children in a reputedly malarious region of the Southern United States. Phillips and Jefferson Counties, Arkansas, were the malarious areas selected. The non-malarious areas were Fulton and Montgomery Counties and Harlem and New York City in New York, and communities in the vicinity of Boston and New Bedford, Massachusetts; no endemic malaria has occurred in these localities for at least 20 years. In all, 6,456 children were examined, 4,571 white and 1,885 Negro. The prevalence of palpable spleens in Negro children is much lower than in white children. The percentage of Negro children with spleen palpable on deep inspiration was 5·3 in the malarious areas, 3·8 in non-malarious areas; of larger spleens the percentages were 1·0 and 1·1. These figures give combined rates of 6·3 and 4·9. The difference is small and indicates that Negro children should not be included in spleen surveys in places in the Southern States where endemicity is low. For white children the percentage of children with spleens palpable on deep inspiration in malarious areas was 12·2 and in

non-malarious areas 10·8; for larger spleens the rates were 11·1 and 3·2, a significant difference. It would seem that PDI spleens [palpable on deep inspiration only] should be disregarded in surveys of places of low malaria endemicity. Palpable spleens were slightly more frequent in children with a history of recent illness, measles, chickenpox, etc., than in other children.

It is interesting to note that, ignoring spleens palpable only on deep inspiration, enlarged spleens were more frequent in New York children, 3·7 per cent., than in Massachusetts children, 1·0 per cent. Both localities are free from endemic malaria.

Nearly all the children examined were between 5 and 12 years of age.

Norman White.

SPICER, S. S. **The Spleen Survey as applied to the Measure of Malaria in the United States—a Review of the Literature.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 165–82. [Numerous refs.]

During the war a thick blood film survey was carried out throughout the endemic malaria areas of the United States; 100,000 thick films were examined. Less than 0·2 per cent. of these were positive, and nowhere was the rate high enough for checking the results of malaria control measures. At the same time in Florida 20 to 25 per cent. of school children were found to have palpable spleens, though less than 1 per cent. had positive blood slides. Partly to explain this situation, the author has made a study of the literature to determine the value of splenometry in the conditions of low endemicity prevailing in the United States. Among the results of the inquiry are the following conclusions:—

A recent epidemic of one of the childhood diseases, and possibly a high rate of infections of the upper respiratory tract, may increase the spleen index. A proportion of apparently healthy children have spleens that are palpable on deep inspiration. Spleen rates as high as 15 per cent. may occur in the absence of malaria; these will be almost all PDI spleens [palpable on deep inspiration only]. Spleen rates above 15 per cent. are probably significant of malaria. A fall in the malaria rates over several years causes a quicker decline in parasite rates than in spleen rates. The spleen index in a community may remain high for several years after a malaria epidemic, partly as a result of relapses, and thus reflects the rate of transmission during the preceding several years. Quinine medication causes a reduction in spleen mass. Spleen rates are influenced by race, age and parasite species. Greater enlargement occurs in the white than in the coloured race, and in children than in adults.

Norman White.

SASPORTAS, L. Paludisme autochtone. L'épidémie de Camargue. [**Indigenous Malaria: the Camargue Epidemic.**] *Rev. Paludisme et Méd. Trop.* 1945, Apr. 15–May 15, v. 3, Nos. 15–16, 81–3.

This is a brief account of an epidemic of malaria in Camargue in 1943, and is based on a report published by J. SAUTET in the journal *Marseille Médical.* Camargue is the region enclosed by the two main branches of the river at the mouth of the Rhône, the only French delta. The inhabitants have always led a somewhat precarious existence in this low-lying tract, with its numerous marshes of varying degrees of salinity. Mosquitoes are abundant and malaria was endemic, but the disease had been very little in evidence during the previous decade; local inhabitants said that it had almost disappeared. The outbreak reported occurred in September 1943. There were 177 cases recorded among the inhabitants of les Saintes-Maries-de-la-Mer and adjacent farms, hospital patients at Arles, Annamite labourers employed in the recently created

rice-fields, Russo-Polish workers, and young workers who had come to help gather the grape harvest. Sautet considered that this number represented not more than half the real incidence. All were *P. vivax* infections of an extremely mild type which showed no tendency to relapse. Blood examination showed gametocyte carriers to be exceedingly rare; this, according to Sautet, is characteristic of places in which malaria is in process of disappearing. The vector was *A. maculipennis* var. *cambournaci*; it was abundant but not noticeably more so than in previous years. The local population blamed the ricefields, but the vector species was not found breeding there. The indigenous population of Camargue has evidently a high degree of resistance to the local strain of *P. vivax*. The author suggests that susceptible arrivals should take prophylactic quinine during the transmission season. *Norman White.*

Guhl, R. Zwei Fällevon autochthoner Malariainfektion in der Schweiz. [**Two Cases of Autochthonous Malaria in Switzerland.**] *Schweiz. med. Woch.* 1946, Jan. 26, v. 76, No. 4, 67–9, 1 fig. [14 refs.]

Polumordvinov, A. D. [**Highland Malaria in Southern Tadjikistan.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 18–20. [In Russian.]

The author reports the occurrence of endemic malaria due to *Plasmodium vivax*, *P. falciparum* and *P. malariae*, at altitudes up to 2,750 and 2,850 metres [=*ca.* 8,920–9,248 feet] above sea level in the mountains of Southern Tadjikistan (Middle Asia). These altitudes represent practically the limit of human settlement in the region in question. *C. A. Hoare.*

Garcia Sastre, L. Notas sobre el paludismo en la isla de Gran Canaria. [**Notes on Malaria in the Island of Gran Canaria.**] *Rev. Sanidad e Hig. Publica.* 1945, Apr., v. 19, No. 4, 257–71, 7 figs. (2 on 1 pl.).

It is almost certain that malaria has existed in the Island of Gran Canaria since very ancient times. Recorded information as to its extent and distribution is scanty. Climatic conditions are eminently favourable for anophelines, and travellers' records of 1775 and 1803 refer to the great prevalence of tertian fevers in the island. Parts of it, however, remain free from malaria. In the capital, Las Palmas, no anophelines were found among 18,826 mosquitoes examined; the few cases of malaria that occurred there in 1944 were all due to infections contracted elsewhere. In the south and centre of the island malaria has long been endemic. Medical reports refer to the large spleens and earthy complexions of some of the inhabitants, notably the children, but without other noteworthy clinical manifestations of malaria.

During the last three months of 1941 an outbreak of malaria occurred in a labour force engaged on constructional work between Fataga and Maspalomas. There were 77 cases. The source of infection may have been a man who contracted malaria in the neighbourhood of Seville. No further cases were reported during the first eight-months of 1942, but the closing four months of that year witnessed a second outbreak of 113 cases in localities adjacent to the infected area of the previous year. In June 1943, malaria reappeared in the north-east and south-west of the island and the ensuing epidemic involved 8 of the 21 administrative divisions. In all, 2,164 cases were recorded in 1943, the highest incidence being in the middle of the southern half of the island. During 1944 cases were reported in every month of the year; in fact there was only one week, in February, in which no new case was notified. The total cases for the year numbered 3,978, and 13 of the 21 *municipios* were involved. Once again the *municipios* of San Bartolomé and Santa Lucia, in the south and centre, suffered

most: here the incidence was equivalent to 190 and 180 per 1,000 of the population. The north-east of the island escaped. The maximum incidence in 1944 was in September, 971 cases, and the lowest in February and March, 26 cases each. Some of the greatly increased incidence in 1944 as compared with the previous year may have been due to the fact that the local medical profession had become more malaria-minded as the result of circulars, propaganda and the like. Of 3,406 cases in 1944, *P. vivax* was responsible for 1,722, *P. falciparum* for 1,660 and mixed infections for 24. *P. malariae* was not observed.

Work with regard to the malaria vectors has not been completed. It would seem that the vectors belong to the *myzomyia* group, probably *A. hispaniola* and *A. sergenti*. Although no anopheline breeding could be found in the urban area of Las Palmas, important breeding places were found in four localities at distances of no more than from 6 to 12 kilometres away.

In view of the rapid spread of infection to places that have been hitherto immune it is not unlikely that the whole island will soon be involved.

Norman White.

NÁJERA, L. La fauna anofélica de las islas Canarias. [**The Anopheline Fauna of the Canary Islands.**] Reprinted from *Bol. de la Real Soc. Española Hist. Nat.* Madrid. 1944, v. 42, 325–6.

The author notes that no anophelines were mentioned by BECKER (*Dipteren der Kanarischen Inseln und der Insel Madeira*, Berlin, 1908), and that the only species found later have been *A. hispaniola* (by Grabham) and *A. sergenti* (by Christophers). He writes of a collection of mosquitoes recently acquired from a collector in the islands and now deposited in Madrid. *Charles Wilcocks.*

LE GALL, R. Le paludisme en Afrique Occidentale Française, au Togo et à Madagascar en 1941. [**Malaria in French West Africa, Togo and Madagascar in 1941.**] *Bull. Office Internat. d'Hyg. Publique.* 1944, May–June, v. 36, Nos. 5–6, 203–24.

This report brings together information concerning the prevalence of malaria during 1941 in each of the Colonies of French West Africa, the mandated territory of Togo and in Madagascar. As elsewhere in the world, complete statistical information regarding morbidity caused by malaria is non-existent. The ratio of malaria cases treated to the total number of sick persons seen in hospitals, dispensaries, infant welfare centres, travelling dispensaries, etc., varies somewhat from year to year and provides some indication of the fluctuations in malaria incidence. Such information suggests that malaria was somewhat more prevalent in 1941 than in either of the two previous years, but the differences were not great. In Madagascar, exceptional rainfall was responsible for very severe malaria; one-third of all sick persons treated were suffering from that disease.

Of special interest in the report is the reference to an inquiry that was carried out in the Comores archipelago, which lies to the west of the northern tip of Madagascar. Malaria was found to be endemic in all the islands, but in varying degrees of severity. Mayotte and Moheli are the islands most severely affected. In Mayotte, spleen rates varied between 40 and 90, and parasite rates from 10 to 18: in Moheli, there were spleen rates of 50 to 80 and parasite rates of 20 to 35. *P. falciparum* infections were predominant. Anjouan is the island least affected; spleen rates varied from 20 to 55. *P. vivax* infections were found in the elevated parts of the island. Great variations of endemicity were found in the island Grande Comore, variations determined in part by the nature of anopheline breeding places, the most important of which are the tanks providing

the water supplies of villages. The three species of *Anopheles* found were *A. gambiae*, *A. funestus* and *A. mauritianus*, the first two being vectors of malaria; these three species are also found on the adjacent north-west coast of Madagascar. *Norman White.*

VISWANATHAN, D. K. **Studies on Malaria in Infants in North Kanara District, Bombay Presidency.** *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 1–38, 4 charts.

The observations recorded were made in Haliyal, population 6,448, and Yellapur, population 1,926, in the North Kanara District, where *A. fluviatilis* is the malaria vector. During the space of one year the blood of 432 infants was examined, 1,628 examinations in all. On the average 45 per cent. of the total infant population were examined each month. The results indicate that the transmission season in Haliyal is confined to the four months September to December. In Yellapur, transmission occurs throughout the year except during the monsoon months July to October. *P. vivax* and *P. falciparum* infections were equally prevalent. *P. malariae* was much less in evidence than it had been in the previous year when malaria was less severe than in the year of investigation. The parasite density in infants was lower than in children of the 2 to 10 age groups, but gametocyte prevalence indicates that infants play an important part in transmission.

Malaria in these two places appears to be responsible for an increase in the number of stillbirths and premature births and for increased neonatal mortality resulting from maternal malaria. It is also an important direct cause of infant mortality. The infant mortality rate of Haliyal was 192 per 1,000 live births.

The author sets out the results of his inquiry in very great detail and discusses at length the value and limitations of such data as he collected in assessing malarial endemicity. *Norman White.*

YACOB, M. & SWAROOP, S. **Investigation of Long-Term Periodicity in the Incidence of Epidemic Malaria in the Punjab.** *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 39–51, 5 charts.

In the absence of reliable data as to the causes of death in the Punjab the authors make use of the deaths ascribed to "fevers" in their elaborate study of malaria periodicity in that Province. Malaria epidemics in the Punjab occur soon after the rainy season and any inordinate increase in deaths ascribed to "fevers" during the last three months of the year affords, in the absence of other unusual epidemics, presumptive evidence of excessive malaria mortality. In studying the fluctuations of malaria mortality from year to year, use is made of an "epidemic figure" which is the ratio of the average monthly number of deaths from fevers during October, November and December to the monthly average of fever deaths of April, May, June and July of the same year. In years of low malaria incidence the epidemic figure should approximate unity.

Epidemic figures for 77 years (1867 to 1943) have been studied. A statistically significant decrease of malaria mortality over this period has been demonstrated and there is a strong indication that epidemics of malaria tend to occur after a period of about eight years. *Norman White.*

FARINAUD, E. & PROST, P. Impaludation et prémunition dans les régions de paludisme endémique de l'Indochine méridionale. [**Malarial Infection and Premunition in Endemic Regions of Indo-China.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 3/4, 93–7.

KAN HUAI-CHIEH. **Malaria Incidence in Two Districts in Western Chekiang, China.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 311–13.

KWOH, C. S. **A Preliminary Report of Malaria Survey in Kweichow.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 314–19.

FAUST, E. C. **Clinical and Public Health Aspects of Malaria in the United States from an Historical Perspective.** *Amer. J. Trop. Med.* 1945, May, v. 25, No. 3, 185–201, 5 figs. (3 maps & 2 graphs). [41 refs.]

This is an informative and interesting account of the introduction, spread and decline of malaria infection in the United States since infection was introduced with the advent of European explorers and settlers and the importation of slaves from Africa two hundred years ago. There is no indication that malaria existed anywhere in North America before then. In the middle of last century most of the settled part of the United States was highly malarious, but even then the hyperendemic centres of infection were in the South. Thereafter, with increasing prosperity, more intensive cultivation, and greatly reduced cost of quinine, the heavily endemic territory began to shrink into the south-east corner of the States. Between 1915 and 1933 there was but little change in the malaria incidence except for the five-to-seven years' cycle of revived intensity. The severe economic depression commencing in 1931 was responsible for a great increase in the intensity and distribution of malaria. This stimulated co-ordinated control measures, which appear to have been responsible for the remarkable decline in malarial mortality which has been continuous and almost uninterrupted since 1933. This decline has been described by the author in annual reports which have been summarized in this *Bulletin*.

The malaria situation to-day is appraised and the potential dangers attendant upon the return to the United States of military forces, merchant seamen and civilians from highly malarious regions is discussed. Both *A. quadrimaculatus* and *A. freeborni* have been shown to be capable of transmitting Pacific and Mediterranean strains of *P. vivax*.

An interesting graph shows how completely malaria was controlled among troops in the United States during the recent world war, and the remarkable decline in malaria morbidity in the army overseas in 1944 as compared with 1943. *Norman White.*

BRITISH GUIANA. **Report of the Malaria Investigations Service of the Medical Department, British Guiana, for the Half Year, July–December, 1944** [GIGLIOLI, G., Government Malariologist]. 48 cyclostyled pp. [14 refs.]

This progress report contains a vast amount of tabulated information concerning spleen and parasite rates in many parts of British Guiana, and the distribution of *Anopheles*. The special report on the incidence and distribution of malaria throughout the colony, which is in course of preparation, will be of great interest. [The Report for 1943 was summarized in this *Bulletin*, 1945, v. 42, 614.]

A survey of the Corentyne Coast was carried out in September and October 1944. Malaria endemicity here is low; of 1,163 children examined, only 1·3 per cent. had enlarged spleens. Parasites were found in 10·7 per cent. of 700 children. In the positive blood preparations parasites were few; in the majority prolonged examination of thick films revealed only one or two ring forms. *A. aquasalis* (*tarsimaculatus*) is very prevalent in this area, and *A. albitarsis* also occurs. Neither of these species appears to be of any importance in the spread

of malaria in British Guiana. Wherever human settlements exist, livestock is abundant, and both of these species show a marked preference for the blood of livestock. No *A. darlingi* were found on the Corentyne Coast.

An appendix to the report, by M. KENNY, deals with inadequate screening as an important factor in spreading malaria. At a mining centre on the Berbice River the population lived in screened wooden houses and in temporary open camps. In the screened houses were numerous cracks and other openings in the floors, walls and roofs, and the doors were often left open after sunset. Hundreds of mosquitoes were captured in the screened houses, 83 per cent. being anophelines, nearly all *A. darlingi*. Blood examination of the occupants showed a parasite rate of 36 per cent. and very numerous gametocyte carriers. Oöcysts were found in 88·8 per cent. of the *A. darlingi* examined. After the institution of daily mosquito catches and the treatment of human carriers, the percentage of infected mosquitoes quickly dropped to less than one per cent. The imperfectly screened houses had been mosquito traps. *Norman White.*

HENDERSON, J. M. **A Discussion on Caribbean Malaria Control.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 189–200, 5 figs.

This is a short general survey of malaria conditions prevailing in the islands of the Greater and Lesser Antilles and in the Guianas. The author directs attention to the large amount of research work that remains to be done, the multiplicity of problems awaiting solution, and the opportunities the Caribbean offers to the enthusiastic malariologist. *Norman White.*

CAUSEY, O. R. & MELLO, G. B. **Malaria in the Amazon Valley of Brazil during 1942 and 1943.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 323–7, 1 map & 1 graph.

Hitherto but little information has been published regarding malaria in the Amazon Valley, a fact which enhances the interest of this contribution.

The Brazilian portion of the Amazon valley, elliptical in shape, covers 3,800,000 square kilometres. The country is remarkably flat. Belem near the coast is 14 metres above sea-level; the elevation of Iquitos, Peru, 3,200 kilometres up the valley, is only 100 metres. Much of the land is flooded. The population of about 1,500,000 live mostly near the navigable rivers, in huts built in piles above the mud and water, in small villages on knolls surrounded by water, or in towns on upland plateaux. Rarely do the people attempt to grow their own food; there is usually a food shortage with consequent malnutrition made worse by widespread intestinal parasite infestation. There are wet and dry seasons, but rain falls in every month. The average annual rainfall in Manaus is 1,995 mm. and in Belem 2,805 mm.

A malaria parasite survey was made in December 1942, a season when malaria rates are expected to be at their lowest. Thick blood films were taken from about 6 per cent. of the population of Belem, from about 20 per cent. of the population of small towns with more than 1,000 inhabitants, and from 30 per cent. of the population of smaller towns. The survey was restricted to towns accessible by air, boat or train. In all, 19,629 blood smears were examined; malaria parasites were found in 979, a parasite rate of 5 per cent. For children of the 1 to 9 age group it was 7·1. *P. falciparum* infections numbered 407 and *P. vivax* 573.

The second survey was carried out at the end of the wet season in June 1943, when 27,103 persons from 37 towns were examined. Instead of the expected rise in incidence the survey showed a parasite rate of only 3·3 per cent. This

may be due to the fact that after the first survey large quantities of atebrin were distributed throughout the valley, and anti-mosquito work had been started in several localities.

Anopheles darlingi is the chief vector of malaria throughout the valley. *A. aquasalis*, another vector, is found near the coast. *A. darlingi* is dependent on lakes or ponds for its survival during the dry season. In an exceptionally dry season these may dry up and *A. darlingi* may disappear altogether. There are some malaria-free areas which may be so explained. When reintroduced, *A. darlingi* may cause severe epidemic malaria in such places. *Norman White.*

Brug, S. L. Exo-Erythrocytaire malariaparasieten. [**Exoerythrocytic Malaria Parasites.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1941, June 14, v. 85, No. 24, 2745–52, 2 pls. (1 coloured) & 1 chart. [Numerous refs.] English summary (8 lines).

The paper describes certain intracellular bodies which were found in smears of the lung of a case of general paralysis which was treated by infection with *Plasmodium vivax*. Death occurred ten days after the intravenous inoculation of the parasites and six days after the first appearance of these in the patient's blood. They were also present in the blood at the time of death. A post-mortem examination was made two days after death, the body having been kept meanwhile in the cold chamber. Smears were made from a number of organs, but it was only in a smear of the lung that anything resembling exoerythrocytic developmental forms of the malarial parasites was found. Three such forms, illustrated in a coloured plate and in microphotographs, were found, all within cells of the endothelial type. The smallest form was a darkish blue body, 3–4μ in diameter, containing four large and three small red-staining masses. It lies in the cytoplasm of a cell about 20μ in longest diameter. The other two forms, which are in somewhat larger cells, are of a different nature. They were both found in the same microscopic field. The cytoplasm of each cell is dotted, over the greater part of its extent, by red-staining masses, some of which are the size of those in the small structure first described, others are larger and some are smaller. The cytoplasm of the cell is not uniform, areas of dark blue being interspersed with less deeply staining areas. In some cases a darkish blue ring is associated with one of the red masses, giving a resemblance to a malarial ring. The number of red masses in each cell is 40 to 50.

The question asked by the author is: are these appearances due to the presence in endothelial cells of malarial parasites or are they the result of cell metabolism? It is remarkable that the three forms described are the only ones seen in all the films examined after many hours of search, and that the two large ones were in the same field. In the larger forms there is no clear demarcation between parasite and cell but this might be due to the fact that segmentation into separate merozoites had already occurred and that their outlines are somewhat obscured—a not unusual appearance in the case of the multiple infection of the cytoplasm of large cells by small parasites. It is perhaps a coincidence, if the red bodies are nuclei of merozoites, that both the larger cells contain parasites in the same stage of development.

However this may be, it is clear that the illustrations bear a striking resemblance to appearances which may be seen in smears of organs containing the exoerythrocytic forms of bird malarial parasites. [The reviewer has re-examined certain of his own films, which show these developmental forms, and he has to admit that had the forms depicted by the author occurred in these films he would not have hesitated to call them exoerythrocytic forms, but this is in films in which many of the parasites show a clear demarcation between

the cell cytoplasm and that of the parasite, so that the occurrence of others in which this demarcation is less clear would not be remarkable. A point worthy of note is that in the cytoplasm of the cell containing the small parasite there are two or three red bodies which cannot be of a parasitic nature, though they bear a resemblance to the red bodies in the other two cells. A resemblance of certain blue areas to malarial rings has been mentioned, but malarial merozoites in endothelial cells are not of the ring form, which is the stage adopted only after invasion of the red blood corpuscle. On the whole, therefore, the reviewer agrees with the author that the structures which are the subject of his paper bear a resemblance to exoerythrocytic forms of bird malaria, but that it is impossible to assert dogmatically that they are the corresponding stages of development of *Plasmodium vivax*. The author is to be congratulated on his exhaustive search, and on the coloured drawings which illustrate his paper and which are undoubtedly faithful representations of the cells they depict.] *C. M. Wenyon.*

Boyd, M. F. **On Difficulties arising in the Experimental Propagation of Falciparum Malaria.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 293–306.

Plasmodium falciparum has been used at the Florida State Hospital since June 1932, largely for the inoculation of coloured patients. The continued propagation of this species by natural passage has proved much more difficult than that of *P. vivax*. Breaks from inoculation failures have occurred in all strains used. In a closely reasoned paper the author analyses the conditions in which these difficulties have arisen.

Failures to infect have occurred though the mosquitoes used were subsequently shown by dissection to have been infected. The presence of sporozoites in mosquitoes that fail to infect indicates that the gametocyte level in the patient from whom the mosquitoes were infected is not a factor. Resistance of the patient has not often been responsible for failure, as was shown by the results of subsequent reinoculations. Increasing age of sporozoites (the period elapsed since the completion of the extrinsic incubation period) has been associated with an increasing proportion of failures, but failures have occurred with quite young sporozoites. It would appear that the recent ingestion of quinine by the patient on whom the mosquitoes are infected may impair the vitality of the resulting sporozoites.

When some of the strains used were propagated by intravenous inoculation of infected blood, their capacity for producing gametocytes deteriorated, sometimes suddenly, sometimes gradually. The phenomenon is not attributable to the resistance of the patient or to the administration of quinine. The deterioration persisted through subsequent passages.

A summary does small justice to this paper. *Norman White.*

Watson, R. B. **Observations on the Transmissibility of Strains of *Plasmodium vivax* from Pacific War Areas by *Anopheles quadrimaculatus*.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 315–21.

Six strains of *P. vivax* were obtained from soldiers who had presumably acquired their infections in Pacific war areas, by injecting their blood into patients requiring malaria therapy. Morphologically, five of these strains differed in no way from the indigenous McCoy strain in general use for treatment, but the ring forms of one strain resembled *P. falciparum* trophozoites; the subsequent development of amoeboid forms revealed their identity. Some of the patients with histories of previous *P. vivax* infections offered considerable resistance to the Pacific strains, four patients being refractory.

A. quadrimaculatus were fed on these patients with Pacific infections. Sporozoites were found in mosquitoes fed on patients infected with three of the six strains. The failure of three strains to infect mosquitoes may have been due to the climatic conditions prevailing at the time of experiment; it was excessively hot and dry, temperature 84°F. and relative humidity 53 to 56. Sporozoite transmission of three strains was successful. In some cases mosquitoes were infected, though microscopic examination revealed no gametocytes at the time of the infective feed.

It is concluded that some at least of the Pacific strains of *P. vivax* can be transmitted by *A. quadrimaculatus*, which seems to be, however, a somewhat less efficient vector of these strains than it is of the McCoy strain.

Norman White.

WATSON, R. B. **On the Probability of Soldiers with Pacific** *Plasmodium vivax* **Malaria infecting** *Anopheles quadrimaculatus*. *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 183–8.

Batches of 25 newly emerged *A. quadrimaculatus* were applied to patients with *P. vivax* infections, acquired in the Pacific war area, without regard to gametocyte levels. After incubation for 15 days in an air-conditioned room these mosquitoes were examined for salivary gland infection. For 1,426 mosquitoes fed on 117 cases (87 patients) the infection rate was 11·8 per cent. The highest infection rate was obtained in mosquitoes which had been fed on patients with parasite relapses without fever. Individuals experiencing their 6th to 15th relapses were twice as likely to infect mosquitoes as were individuals with earlier or later relapses.

Norman White.

ROUBAUD, E. Influence du développement plasmodien sur la fécondité des moustiques hôtes. [**The Influence of Plasmodial Development on the Fecundity of Mosquitoes.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 300–304.

CIUCA, M., BALLIF, L., CHELARESCU, M. & CRISTESCU, A. Capacité d'infection du sang des porteurs de gametocytes de *Plasmodium falciparum* pour *Anopheles maculipennis* (*V. atroparvus*). [**Infective Capacity of** *Plasmodium falciparum* **Gametocyte Carriers for** *Anopheles maculipennis atroparvus*.] Reprinted from *Bull. Sect. Sci. Acad. Roumaine*. Bucharest. 1942, v. 25, No. 2, 96–102.

Thirty-six *P. falciparum* gametocyte carriers were used for the infection of laboratory-bred *A. maculipennis atroparvus*. Twenty-three of these patients had been infected with virulent blood, 9 had been infected with sporozoites and 4 were cases of natural infection. The strain used for the infection of 32 patients had been kept going for 14 years in the malaria-therapy station.

The researches show that 50 per cent. of these gametocyte carriers were incapable of infecting a lot of mosquitoes in the conditions of the experiment (one infecting feed only). Two cases on which mosquitoes were fed 10 times show the importance of the number of infecting feeds in producing infection.

The infective power of the blood is independent of the manner in which infection was contracted (virulent blood or sporozoites).

Three of the four gametocyte carriers who had naturally acquired infections successfully infected mosquitoes, a very much higher rate of infectivity than that shown by patients infected with the laboratory strain. The vitality of the gametocytes of these naturally acquired strains appeared to be much higher than of those of the therapy strain.

Norman White.

GARNHAM, P. C. C. **The Rôle of *Anopheles pharoensis* Theobald in the Transmission of Malaria in Kenya Colony.** *Ann. Trop. Med. & Parasit.* 1945, Oct. 10, v. 39, No. 2, 63–5.

Anopheles pharoensis is a carrier of malaria in Egypt, the Sudan, Uganda, the Belgian Congo and Southern Nigeria ; in Egypt it is an important carrier. In Northern Nigeria and Kenya no infections have been found.

A. pharoensis has a patchy distribution in Kenya, at altitudes between 2,000 and 3,000 feet. It breeds in large numbers in swamps around lakes, and also in overgrown drains and streams. Adults are rarely found in large numbers in human dwellings. At Kisumu, where the observations recorded were carried out, they formed from 0·7 to 4 per cent. of the total anopheline day catches in huts ; for night catches the percentage was 10. They mostly enter huts between midnight and dawn. The salivary glands of 1,334 female *A. pharoensis*, and 33 midguts, were examined. Neither sporozoites nor oöcysts were found. The species feeds on man ; the stomach contents of 10 engorged females all gave positive precipitin reactions with anti-human serum. The maxillary index of local specimens was 14·6, which suggests zoophilism. The length of life of the species is sufficient to develop infection. The author suggests that where *A. pharoensis* is an important vector of malaria, a variety of the species, and not the type-form, is concerned. *Norman White.*

VINCKE, I., PARENT, M., BERTEAUX, M. & DE MEULENAERE, J. Note sur la biologie de *Anopheles dureni* Edw. [**A Note on the Biology of *Anopheles dureni* Edw.**] *Bull. Ass. Congolaise des Anciens Étudiants de l'Université de Liége.* 1945, Oct., No. 5, 30–39, 1 chart.

Anopheles dureni is a common day-biting mosquito near Elizabethville in the Belgian Congo. It is not found at all in human habitations, but is commonly captured among trees near water. Biting takes place throughout the hours of daylight, but ceases completely at nightfall ; other species, for instance *A. funestus*, were observed during the same investigation to bite almost entirely by night.

Dissections were made of 736 adult *A. dureni*, some on the day of capture, some after five days' captivity. Approximately 9 per cent. were infected with malaria parasites, most of them having salivary gland infections.

Larval breeding places are described. Shaded sections of rapidly-running streams are the most important. Both larvae and adults are commonest in January and February, and scarcest from March to September.

Kenneth Mellanby.

WEATHERSBEE, A. A. & BOHART, G. E. **Observations on the Nocturnal Activity of Anopheles and certain other Mosquitoes in Eastern Puerto Rico.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, June, v. 19, No. 4, 626–34, 1 chart. [Spanish version 635–42.]

Three experiments were conducted in an attempt to determine the time of greatest activity of mosquitoes in an area of Eastern Porto Rico.

Horse-baited traps were established in three localities, and hourly collections were made from them from 5 p.m. until morning. The first experiment ran from October 30th to November 10th, 1942, the second from November 18th to 29th, 1942, and the last from January 19th to 30th, 1943.

Three species of *Anopheles* were taken : *A. albimanus* (1,330), *A. grabhami* (347), and *A. vestitipennis* (32). There were also five species of *Culex*, three *Aëdes*, two *Psorophora* and one *Deinocerites*.

The hourly figures are tabulated and show that *Anopheles albimanus* was more active between 8 p.m. and 3 a.m. than during either the earlier or later hours and that the peak time of entry lay between 10 p.m. and 1 a.m. The numbers of the other anophelines do not indicate any pronounced peak of activity.

The common mosquitoes *Culex bahamensis, nigripalpus, quinquefasciatus* [*fatigans*], *Aëdes taeniorhynchus* and *Psorophora confinnis* readily entered the traps at all hours of the night. *H. S. Leeson.*

Rubenstein, A. D., Shulman, M. H. & Merrill, D. **The Hazard of Transfusion Malaria after the War.** *New England J. of Med.* 1945, Aug. 23, v. 233, No. 8, 234–7.

Since 1929 twelve cases of post-transfusion malaria have been reported in Massachusetts. On the assumption that the chance of such happenings may be increased in the future owing to the greater number of potential donors who have served in malarious regions, the authors give details of the twelve cases that have occurred to emphasize the risk of post-transfusion malaria. Of the 12 infections 9 were due to *P. malariae*, 2 to *P. vivax* and one to an undetermined species. The interval between the transfusion and the onset of symptoms varied between 10 days (*P. vivax*) and 111 days (*P. malariae*). The time elapsed since the donor was last in an endemic malaria region was determined in 5 cases; the longest period was 27 years, the shortest 12 years. Attempts to demonstrate malaria parasites in blood smears of the donors were made in 7 cases but were successful in only two. *Norman White.*

Talice, R. V. & Mackinnon, J. E. Paludismo accidental por transfusión [**Transfusion Malaria.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1945, Nov., v. 27, No. 5, 473–81. [29 refs.] English summary.

" Two accidental cases of transmission of malaria by transfusion of whole blood are recorded.

" Both cases were produced by *Plasmodium malariae.*

" One of the donors acquired malaria in Africa 9 years before and the other in Italy 7 years before.

" The infective area of malaria endemicity does not reach the Republic of Uruguay. Consequently, in order to avoid accidental transmission of malaria the authors emphasize the advice and conclusions given by Hutton and Shute, which may be easily accomplished in Uruguay, that only donors who have never left the country should be used."

Ciuca, M., Ballif, L. & Chelarescu, M. Contribution à l'étude de l'immunité dans l'infection paludéenne expérimentale. Observations recueillies sur 41 sujets immunisés. [**Contribution to the Study of Immunity in Experimental Malaria Infection : Observations on 41 Immunized Individuals.**] Reprinted from *Arch. Roumaines Path Expér. et Microbiol.* Bucharest. 1943, Jan.–Dec., v. 13, Nos. 1/2, 45–122, 41 figs. [111 refs.]

The receipt of this interesting study, admirably produced, affords welcome evidence that the scientific work of Ciuca and his colleagues triumphantly surmounted difficulties imposed by war conditions, and has been most profitably carried on.

The paper opens with a useful summary of contributions to the literature of acquired immunity against human, bird and monkey malaria. The 111 references in the bibliography are an indication of the comprehensiveness of

this summary. [Some recent work was evidently inaccessible to the authors; for example Boyd & Kitchen (1943), this *Bulletin*, 1943, v. 40, 818, is not quoted.]

The observations recorded relate to 41 patients who, after having been submitted to malaria therapy, were kept under control for from 4 to 14 years. They were immunized by repeated inoculations of virulent blood or, more rarely, of sporozoites. After the period of immunization, inoculations were suspended for some years during which time monthly examinations of blood were made. The duration of immunity was gauged either by determining the persistence in the body of parasites, by transfusion of blood into a susceptible individual, or by a direct test of the immunity by a fresh injection of virulent blood.

P. malariae confers a more lasting immunity than the other two species of human plasmodia. The persistence of an immunity against *P. malariae* in the absence of parasites from the body detectable by transfusion certainly does not rule out the possibility of a humoral or cellular immunization.

In the immunity conferred by *P. vivax* the rôle of premunition is more in evidence, but in 3 of 14 of the cases recorded, immunity persisted though no latent infection could be demonstrated. When the higher frequency of positive transfusions in *P. vivax* infections is considered it must be remembered that the patients were not protected from possible fresh natural infections.

From the point of view of efficacy and duration of immunity conferred by repeated inoculations, *P. falciparum* comes last. The severity of this infection necessitates earlier antimalarial treatment after the first inoculations; the infection is of shorter duration than the other two and there is therefore a shorter antigenic saturation of the organism. All the same a certain resistance persists in patients immunized with *P. falciparum* inoculations, as evidenced by the fact that spontaneous recovery may take place from infections given several years later. *Norman White.*

Hunter, T. A. A. **Fever in a Hyper-Endemic Malarial Area. A Critical Analysis of 2,913 Cases.** *Indian Med. Gaz.* 1945, May, v. 80, No. 5, 247–55.

A forward Treatment Unit in one of the most malarious areas of the Assam-Burma border, in the height of the transmission season, received up to capacity all cases of fever, British and Indian, in which no definite diagnosis had been made. Diagnosed cases of malaria were also received, but these were few in number. There were in all :—

	British	Indian	Total
Proved malaria	643	1,563	2,206 (76%)
Clinical malaria	41	45	86 (3%)
Not malaria	177	444	621 (21%)

The author protests against the diagnosis of clinical malaria and the commencement of antimalarial treatment before diagnosis has been confirmed. Of the cases of clinical malaria, admitted as such, not more than a sixth eventually justified that diagnosis. The facile diagnosis may be dangerous; in this series five cases of pneumonia were overlooked by a too easy resort to it. Severe types of malaria are relatively uncommon, 2·4 per cent. in this series, and fulminant types are rare. In all severe cases parasites were plentiful in the peripheral blood. No evidence was forthcoming of the existence of that

" bogey man of the medical officer," the cerebral case of malaria with persistently negative blood slides. The thick drop method of blood examination is very sensitive. In the series of cases reported, parasites were found on the first examination in 81 per cent. of British cases and in 90 per cent. of Indian cases; on second examination, 12 hours later, parasites were found in a further 8 and 6 per cent., respectively. There is, moreover, in military practice an important practical objection to the diagnosis of malaria on insufficient grounds. A patient suffering from " malaria " is absent from duty for 15 days; the average " non-malaria " patient in this series was fit for duty again within the week.

The percentage incidence of species of plasmodia in this series were :—

	P. falciparum	*P. vivax*	*P. malariae*	Mixed
British troops ...	30	64	1	6
Indian troops ...	43	47	1	9

Most British troops had been taking mepacrine as a suppressive, most Indian troops had not. This may have been a factor in determining the greater relative prevalence of *P. falciparum* among Indian troops.

In nearly two-thirds of the malaria cases the spleen was not palpable. The spleen rate was higher among Indians.

In 70 cases in which a suspicion of malaria persisted after three negative blood examinations, adrenaline injections were used; as a result parasites were found in seven patients; adrenaline is a useful diagnostic aid. Sternal puncture, a simple procedure, was used 20 times; it was not useful as an aid to diagnosis. Spleen puncture was performed three times; it revealed one *Leishmania donovani* infection, and one mixed *P. falciparum* and *P. vivax* infection. The procedure is, of course, not suitable as a routine diagnostic measure.

Only eight British and four Indian patients developed cerebral symptoms. There were no algid cases, and there were no deaths. A dose of quinine was given intravenously without delay to all patients with *P. falciparum* infections who had symptoms of any degree of severity or in whose blood there was high parasite density. *Norman White.*

Bystrov, P. V. **[Malignant Fulminating Tertian Malaria, according to Observations of Tambov Pathological Department.]** *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 21–5. [In Russian.]

The author, in 1927, was the first to draw attention to the occurrence in the Soviet Union of a fulminating, deadly type of " benign " tertian malaria, affecting chiefly children. Since then outbreaks of this form of malaria have been regularly recorded [this *Bulletin*, 1943, v. 40, 436, 668; 1944, v. 41, 257, 823]. In the present paper the author records post mortem observations on 100 fatal cases of *P. vivax* malaria, carried out by him in the course of the last 20 years, at the prosectorium of the Tambov hospital. Outbreaks of this form of malaria occur regularly every year in the spring (March, April, May), the majority of cases being in children between the ages of 4 and 16, though in seven cases the victims were adults.

The clinical picture was similar in all known cases. The majority had previously suffered from malaria, and usually the attack which culminated in death was the second one. This attack—which was accompanied by repeated vomiting, followed by loss of consciousness, convulsions and death—usually started suddenly and lasted only several hours. In all cases the diagnosis was confirmed

by the finding of typical *P. vivax* in the blood and organ smears, the predominant stages being schizonts. The histopathological picture revealed no special features. In distinction to the comatose form of malignant tertian malaria, the brain never showed any macroscopic evidence of pigmentation. Among the characteristic changes, the author notes: (1) enlargement of the spleen; (2) cerebral oedema, and (3) increased intracranial pressure. Microscopical examination reveals a moderate number of parasites and slight pigmentation, chiefly in the spleen and liver. The enormous accumulations of these elements, characteristic of malignant tertian malaria, are never observed.

The author attributes the grave symptoms and fatal termination in this form of malaria to an acute cerebral oedema, accompanied by increased intracranial pressure, which leads first to irritation and finally to paralysis of the nerve centres. This effect may be due both to mechanical and chemical causes, while the oedema itself is visualized as a local allergic reaction on the part of the nervous tissue as the result of sensitization by the products of decomposition of foreign proteins provided by the parasites. *C. A. Hoare.*

COGGESHALL, L. T. **Malaria and Filariasis in the Returning Serviceman. The Ninth Charles Franklin Craig Lecture.** *Amer. J. Trop. Med.* 1945, May, v. 25, No. 3, 177–84.

The information in this lecture is based on observations of more than 3,000 service men, returned from overseas, in the Marine Barracks, Klamath Falls, Oregon. Most had acquired malaria in the Pacific war area. The records show that initial infections had frequently been with *P. falciparum*, but only *P. vivax* infections were found at this station. Three men, who had been admitted for filariasis, experienced their first malarial attack on the station, where there is no possibility of local infection. In one of these cases eight months had elapsed since the man had been in an endemic area and had discontinued suppressive mepacrine. Infections with Pacific strains of *P. vivax* are very prone to relapse. Fifty-seven per cent. of the men under observation had had more than 14 acute attacks; some had had as many as 40. The recrudescences have a certain rhythm; many men could predict within a week when the next attack would occur. There was a remarkable absence of malarial cachexia. Splenomegaly was noted in less than 5 per cent. of the men, even after 20 to 30 recrudescences. Immediately after the acute attack spleens were palpable in about 8 per cent. Anaemia was conspicuous by its absence; after six weeks at the station (the altitude of Klamath Falls is 5,000 feet) the average red blood count was 5,300,000. Except for persistent headache in some cases, there was no disability between acute attacks of fever. Finally, Negroes who are very refractory to U.S. strains of *P. vivax*, are very susceptible to Pacific strains.

The men were put on full duty, military training, recreational, educational and vocational activities. This was regarded as important. Physical fitness was quickly regained and the development of " hospitalitis " avoided. Even South Pacific malaria is a self-limited disease. The rate of recrudescence had a downward trend in the malaria that was still active after three years from inception.

There was a large group of men with *Wuchereria bancrofti* infection, which in 96 per cent. of cases had been contracted in the Samoan group of islands. The incubation period, from the first possible exposure to infection to the appearance of initial symptoms, averaged nine months. The clinical signs were lymph-oedema, lymphadenopathy and lymphangitis:—in the neck (2 per cent.), upper extremities (30), lower extremities (9), scrotum (1), spermatic cords (15), and testes (18 per cent.). The manifestations were very mild. Microfilariae were not found in any man in the station; occasional eosinophilia was the only abnormal

finding on blood examination. Temperatures were normal, and a chronic cough was the only symptom. Occasionally the oedema, lymphangitis and muscular soreness flare up but for a few days only, and attacks become less and less frequent. It has been necessary to admit to hospital only one man in 800 for filariasis. The psychic element in these cases is prominent and patients need reassuring ; all accumulated evidence shows that filariaris will not result in permanent disability in such cases. Mental and physical rehabilitation of these cases is most important to avoid unnecessary invalidism.

There is no likelihood that filariasis will gain a foothold in the United States. [See also ZELIGS, this *Bulletin*, 1946, v. 43, 53]. *Norman White.*

KAPLAN, A. **Recurrent Headache resultant from Malaria.** *J. Amer. Med. Ass.* 1945, Oct. 27, v. 129, No. 9, 612–13.

An American Marine who had apparently been exposed to malarial infection in the Pacific area between April 1942, and the time of his admission to the ship's sick bay in December 1943, complained of severe occipital headaches of three weeks' duration which prevented sleep and had led him to drink alcohol to excess in the hope of getting some relief.

Very thorough physical and psychiatrical examinations, radiography of the skull, Kahn tests of the blood and cerebrospinal fluid, chemical examination of the blood and cerebrospinal fluid, the extraction of two lower molar teeth, all led to no diagnosis during two months of " hospital study " ; he was discharged unimproved and at his own request returned to duty. No examination of blood films for malaria parasites was made.

His headaches continued and prevented sleep, and after trying to carry out his duties for five days, he was again admitted for further study. This produced no diagnosis except one of psychoneurosis by the psychiatrist who reported fully on his mental state. Again no blood films were examined. After two months he was admitted to a hospital " on the mainland " and was again submitted to exhaustive physical and psychiatrical examination, together with laboratory studies, but still no examination of blood films was made. The psychiatrist reported that the patient had a desire to do his duty but showed lack of energy and determination ; he appeared to be unhappy.

After a month's leave he was allowed to return to duty and managed to carry on for nine months in spite of recurrent headaches. He was then " returned to the Pacific area " where his headaches continued for eight months and he steadily lost weight for six months. He was admitted to the hospital complaining that his headaches had been very severe for the last month and that he had had chills and fever for 10 days. A blood film showed *Plasmodium vivax*. Treatment with quinine and atabrine cured the chills and fever and his headaches completely disappeared—for the first time during some years.

The author comments that the experience he describes is not altogether unusual and that malaria in the Pacific area is a common disease.

J. F. Corson.

NAGLEY, L. **Probable Relapse of Malignant Tertian Malaria after Thirteen Years.** *Lancet.* 1945, Dec. 15, 773–4.

This is a report of a most unusual case. The patient had been a soldier in India from 1919 to 1928, when he returned to England and since then he has not been out of the British Isles. He had malaria in India in 1928 and a possible relapse in 1932 which was " cured " with one dose of quinine. Thereafter he remained in good health till April 1935, when he fell ill with jaundice, vomiting, bloody diarrhoea and daily shivering attacks. Blood examination

revealed very numerous ring forms of *P. falciparum* and crescents. He recovered. It is incredible that he should have been infected with *P. falciparum* in England thus early in the year. He had never been treated with malaria therapy nor had he ever had a blood transfusion. It is difficult to escape the conclusion that the attack was a relapse 17 years after infection.

Norman White.

Büssow, H. Über Psychosen nach Malaria. [**Malarial Psychoses.**] *Allgemeine Ztschr. f. Psychiatrie u. ihre Grenzbebiete.* 1944, Sept. 25, v. 123, Nos. 3/4, 235–77. [18 refs.]

More than half of this long article consists of a detailed description of the symptomatology of 14 cases of malarial psychoses, of which 10 were associated with benign tertian infection, three with malignant tertian, and one with a mixed benign tertian and malignant tertian.

All the patients were being treated or had been treated with the standard course of atebrin and plasmoquine, but the author does not consider that the treatment was responsible for the illness.

No indication is given of the total number of cases of malaria among which the psychoses occurred except that the author refers to an extensive experience of great epidemics during the war and mentions that the condition is relatively uncommon.

In five cases the onset was during a febrile paroxysm, in eight it occurred one to nine days after defervescence, and in one it was 20 days later. The manifestations were very varied, including mania, anxiety, depression, hallucinations, delusions, and, in three cases, suicidal tendencies.

The duration was very variable, but even in prolonged attacks the prospect of complete recovery is considered to be good. *John W. D. Megaw.*

Menon, T. B. & Veliath, G. D. **Acute Polyarteritis Nodosa in a Case of Malaria.** *Indian Med. Gaz.* 1945, Sept., v. 80, No. 9, 452–4, 7 figs. on 1 pl. [12 refs.]

Babin, Frances & Dulaney, Anna D. **Complement Fixation in Malaria and Syphilis.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 167–73, 3 figs.

The authors have found that not only may malaria be a cause of false positive complement-fixation reactions for syphilis, but that syphilis may be a cause of false complement-fixation reactions for malaria when a phosphate buffer extract of *P. knowlesi* is used as antigen. The human material available for study consisted of 200 patients with relapsing *P. vivax* infections who were clinically and serologically negative for syphilis ; 408 sera giving positive Kahn reactions obtained from the laboratory of a State Health Department, and 22 syphilitic patients with induced malaria. Sera were collected at intervals of 3 to 5 days from the malaria patients ; 1,851 samples were thus collected and on each sample complement fixation tests for both malaria and syphilis were performed simultaneously. Of these, 129 gave positive Wassermann reactions (7 per cent.), and 112 of these 129 sera also gave positive results with the *knowlesi* antigen (87 per cent.). Of the 1,722 sera that gave negative Wassermann reactions 1,105 (64 per cent.) gave positive malaria reactions. Most of the positive Wassermann reactions in malaria patients occur from 6 to 10 days after a malaria attack.

Of the 408 syphilitic sera, taken at all stages of syphilis infection, 14·5 per cent. gave strongly positive reactions and 6·8 doubtful reactions with the *knowlesi* antigen. High-titred syphilitic sera give a larger number of these false reactions than do low-titred sera.

In the 22 syphilitic patients with induced malaria the malaria complement fixation test became positive at the time the first positive blood film was observed, or shortly after, and the titres followed the rise and fall of the parasitaemia. Eighteen of these 22 patients showed a rise in Wassermann titre coincident with the rise of the malaria complement-fixation titre. The relation between fluctuations in the malaria and syphilis complement-fixation titres was striking. *Norman White.*

Robinson, H. M., Jr. & McKinney, W. W. **The Effect of Vivax Malaria on Spinal Fluid and Blood Serologic Test for Syphilis.** *J. Amer. Med. Ass.* 1945, Nov. 3, v. 129, No. 10, 667–8, 1 chart.

One hundred soldiers who were suffering from *P. vivax* malaria, with parasites in the peripheral blood, and who were non-syphilitic, were arbitrarily selected for these studies. They had all been in a malarious region for several months and had been transferred to a malaria-free district three months before the investigation began. Nine were experiencing their first attack of malaria; the others had had from one to sixteen previous attacks. Lumbar puncture was performed and blood taken for serological tests within 5 days after the diagnosis of malaria was made. If the blood test was positive or doubtful the test was repeated at weekly intervals till a negative reaction was obtained. The standard three-tube Kahn flocculation test was performed on all blood specimens, and the spinal fluid was examined with the standard Kahn test, Pandy and cell count. The spinal fluid Kahn reaction was negative in all cases. In two cases the Pandy was reported as "a trace". The cell count was within normal limits in all. The blood serological test for syphilis was positive in 33 patients, doubtful in 11, and negative in 56. Two of the patients with positive reactions were lost from observation. Of the remainder, 26 gave negative reactions after four weeks and all had become negative after 10 weeks. All patients had been put on mepacrine therapy as soon as the diagnosis of malaria was made. There was no apparent correlation between the number of attacks of *P. vivax* malaria suffered and the development of positive serological reactions for syphilis. *Norman White.*

Bruetsch, W. L. **Malaria Therapy in Syphilitic Primary Optic Atrophy.** *J. Amer. Med. Ass.* 1946, Jan. 5, v. 130, No. 1, 14–16, 3 figs. [Refs. in footnotes.]

Fenton, J. C. B. & Innes, J. **A Staining Method for Malaria Parasites in Thick Blood-Films.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Sept., v. 39, No. 1, 87–90.

The staining method described is a modification of the now well-known Field procedure, whereby a thick film is dehaemoglobinized during the staining process which is completed by immersion for 10 to 15 minutes in a corrective Leishman solution. It is claimed that the method ensures optimal staining results for the demonstration of malarial parasites. Those who wish to try the new method must consult the original article for details of the technique and method of preparation of the three staining solutions used.

C. M. Wenyon.

Das Gupta, B. M., Lowe, J. & Chakravarti, H. **M3349 (Paludrine) in the Treatment of Human Malaria.** *Indian Med. Gaz.* 1945, May, v. 80, No. 5, 241–5.

This study of the value of paludrine, an antimalarial compound prepared by Imperial Chemical Industries, in the treatment of malaria, was designed to

determine the toxicity of the drug and the relapse rate after treatment. The difficulty of keeping general hospital patients under observation sufficiently long to determine the relapse rate prompted the selection of malaria patients in the Narkeldanga Relief Camp for Sick Destitutes for the trial. Thirty-one such patients were admitted into the Tropical Diseases Hospital and 75 were treated in the Camp. It is rather unfortunate that patients in such bad physical condition should have been selected.

The drug was put up in tablets each containing 0·2 gm. The dose recommended in the control of attacks of malaria was three tablets a day for seven days. The occurrence of two deaths of patients under treatment in hospital early in the trial caused the subsequent dosage to be reduced to two tablets a day. The two patients who died were both infirm men, of 60 and 65 years of age ; their weights were 86 and 85 pounds, respectively. Whether the toxicity of the drug contributed to death seems to be doubtful.

The authors conclude that paludrine has an action comparable to that of quinine and mepacrine in both *P. falciparum* and *P. vivax* infections, fever being promptly controlled and parasites disappearing from the peripheral blood. In four cases of *P. malariae* infection the action was less marked.

Of 60 patients treated and kept under observation for several weeks, 18 had a clinical relapse from 19 to 56 days after treatment, and seven had a parasitic relapse without fever. The early relapse rate was thus 30 per cent. Some of these " relapses " may well have been fresh infections, for most of the work was done in a camp in a highly malarious area in the middle of a malaria epidemic !

Of 51 patients with *falciparum* infections and observed for several weeks, there was no *falciparum* relapse, but 8 had a return of fever with *P. vivax* in the blood.

In persons in reasonable physical condition, symptoms of intolerance to the drug (such as nausea and vomiting) are slight and present no great difficulty. In persons with complicating diseases, particularly respiratory diseases, the danger of toxic effects is much greater. Three deaths occurred among patients being treated with two tablets a day. Thus there were five deaths in all, but in only one of these was there no serious complicating disease.

Norman White.

Stokes, J. F. **The Treatment of Relapsing Malaria.** *J. Roy. Army Med. Corps.* 1945, Aug., v. 85, No. 2, 75–80, 1 fig. [13 refs.]

The drain on man-power of continually relapsing malaria is more serious than the occasional death from cerebral malaria. The relapse rate in a series of British patients of the 14th Army, known to be relapsing, was 64·7 per cent. over a period of 11 weeks. The author discusses various views that have been put forward regarding the pathogenesis of relapse. In a search for a method of reducing the relapse rate a trial was made of urea stibamine. This was prompted by certain analogies between kala-azar and malaria, but more by two cases that had come under observation. These were two Indians who were suffering from both kala-azar and relapsing malaria ; neither had a malaria relapse while undergoing prolonged treatment with urea stibamine.

Two series of observations were carried out, the first on Indian soldiers, 48 experimental and 50 controls, and the second on British troops, 52 experimental and 52 controls. The observations were made in malaria-free localities.

Every patient received the standard malaria treatment : quinine 10 grains thrice daily for 2 days ; mepacrine 0·1 gm. thrice daily on days 3 to 7 ; pamaquin 0·01 gm., thrice daily for British troops and twice daily for Indian troops, on days 10 to 14. The experimental patients received doses of urea stibamine,

on the 15th, 17th, 19th and 21st days, of 0·05, 0·10, 0·15 and 0·20 gm., respectively. The corresponding doses for Indian troops were 0·025, 0·05, 0·10 and 0·15 gm.

The relapse rates for the control and experimental groups of British troops were almost identical over a period of 91 days, 70·6 and 70·2 per cent. On the other hand urea stibamine appeared to reduce the relapse rate of the Indians who were, however, observed only for 5 weeks. During this time the relapse rate of the control group was 34 per cent. and of the experimental group 6·25 per cent. But in the experiment with British troops, 46 per cent. of the relapses occurred after the fifth week and the author believes that had the Indians been kept longer under observation the relapse rates of the two groups would have more nearly approximated.

The author concludes that urea stibamine is unable to influence the course of relapsing malaria. *Norman White.*

PROKOPENKO, L. I. [**Parasite-carriage of *Pl. vivax* in a New Focus of Malaria subjected to Control Measures.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 3–13, 4 figs. [In Russian.]

This paper deals with the effect of systematic drug treatment upon the incidence of carriers among patients suffering from benign tertian malaria in a new focus of the disease. The observations were made in three villages of the Moscow province during 1940 and 1941. Both clinical cases and carriers were treated with acriquine [mepacrine], the course consisting of three cycles of seven, two and three days, respectively, separated from each other by free intervals of ten days each, the daily dose for adults being 0·3 gm. During the entire period of observation the number of cases of malaria with febrile symptoms exceeded that of symptomless carriers (249, or 79·6 per cent., and 64, or 20·4 per cent., respectively, out of a total of 313 cases). The effectiveness of the treatment was assessed by comparison of 141 patients who had undergone a regular course of treatment, on the one hand, and a group of 46, treated irregularly, on the other hand. In the former group, relapses occurred only in 19·8 per cent., while in the latter 26 (*i.e.* more than 50 per cent.) relapsed. Furthermore, in the first group repeated relapses were more frequent, thus 28 patients had 37 relapses, comprising 23 acute and 14 symptomless cases (carriers). In the second group 26 patients had 48 relapses (27 acute and 21 symptomless). It is concluded that properly conducted regular treatment of malaria leads to a marked reduction in the total number of relapse cases, both acute and symptomless. *C. A. Hoare.*

GALUSHKINA, O. N. [**Malaria Treatment by Irradiated Quinine.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 2, 26–7. [In Russian.]

It has been shown by ROSKIN that quinine irradiated by ultraviolet rays has a more powerful effect upon ciliates *in vitro*, and a more lasting therapeutic action in bird malaria, than ordinary quinine. In the present paper the author records the results of treatment of human malaria with irradiated quinine. The method of preparation is as follows: 10 per cent. solution of quinine hydrochloride is poured out into Petri dishes and irradiated with a quartz lamp at a distance of 30 cm. for five minutes. The solution is then evaporated in a water bath, and the dry powder is administered in daily doses of 0·3 gm. for four days in succession (five days in the case of malignant tertian malaria) followed by three cycles of three days each, with intervals of four days between the cycles.

Of the 30 patients under this treatment, 20 were in the acute stage of the disease, with parasites in their blood (17 benign and 3 malignant tertian cases), while 10 had subfebrile temperatures attributed to chronic malaria, though no parasites were found in their blood. In the last group irradiated quinine brought about only a temporary reduction of the temperature, whereas in the true malaria cases the results of treatment were very promising. As a rule the first dose prevents further paroxysms, except in malignant tertian malaria with daily paroxysms. In the latter case febrile symptoms were sometimes observed two or three days after treatment. As regards the parasites, these disappeared in 2–3 days in benign tertian malaria, while the gametes of *P. falciparum* disappeared after a fortnight. The most important result of this treatment is, thus, the rapid cessation of attacks of fever and the absence of relapses in patients kept under observation up to eighteen months after a course of treatment. *C. A. Hoare.*

GOTTFRIED, S. P. & LEVINE, A. C. **Liver Function Studies on Soldiers under Prolonged Atabrine Administration.** *J. Lab. & Clin. Med.* 1945, Oct., v. 30, No. 10, 853–5. [17 refs.]

Fifty Negro soldiers who had been taking atabrine 0·1 gm. six days a week for 18 months were examined. None had had clinical malaria, syphilis, scrub typhus or jaundice. The tests employed were icterus index, urine urobilogen fibrinogen, serum cholesterol partition, and the oral hippuric acid test. Where the total serum cholesterol values were high, total serum lipid determinations were made. As a check on the fibrinogen results this determination was also performed on 50 other soldiers who had been taking atabrine for only from one to three months.

Several months later, bromsulphalein, cephalin flocculation, and galactose tolerance tests were performed on 50 more soldiers who had also been taking atabrine for from 20 to 24 months. As a control of the sensitivity of the cephalin flocculation test, determinations were performed on 25 soldiers who had been taking atabrine from one to three months.

At a still later date 25 additional bromsulphalein tests were done on soldiers who had been taking atabrine for 30 months.

Plasma fibrinogen was determined colorimetrically. Icterus index was determined by the method of MEULENGRACHT (*Deut. Arch. f. Klin. Med.*, 1920, v. 132, 285); urine urobilinogen by SPARKMAN's method (*Arch. Intern. Med.*, 1939, v. 63, 856); oral hippuric acid test by QUICK's method as modified by KRAUS and DULKIN (*J. Lab. & Clin. Med.*, 1941, v. 26, 729 & 1078). Total serum cholesterol was measured colorimetrically, and free cholesterol by the method of SCHOENHEIMER and SPERRY (*J. Biol. Chem.*, 1934, v. 106, 745). The total lipid content was measured gravimetrically. The bromsulphalein test was done by injecting 2 mgm. per kgm. of body weight and by measuring the retention at the end of 18 minutes. The cephalin flocculation test was done by HANGER's method (*J. Clin. Invest.*, 1939, v. 18, 261), and the galactose tolerance test by the method of JANNEY and ISAACSON (*J. Amer. Med. Ass.*, 1918, v. 70, 1131).

Of all the hepatic function tests employed, only the hippuric acid test gave results indicative of hepatic dysfunction and then in only very few cases. This by itself was not significant. The conclusion is that no subclinical liver damage could be detected among the soldiers studied. *Norman White.*

J. AMER. MED. ASS. 1945, Dec. 15, v. 129, No. 16, 1091–3. **Untoward Reactions attributable to Atabrine.**

This report represents the views of a considerable number of U.S. Army medical experts on cutaneous reactions that have resulted from the administration of suppressive atabrine, notably the "atypical lichen planus syndrome."

The condition was observed in the latter half of 1943 in soldiers who had been evacuated from New Guinea and adjacent islands. The syndrome has been most commonly seen in this area and in Assam and North Burma; elsewhere only few cases have occurred. The incidence of these cutaneous lesions has been low even in New Guinea, and has not constituted an important handicap from the military point of view. Cutaneous reactions have been more frequent in persons who have taken suppressive atabrine in larger doses than the recommended amount, 0·7 gm. per week.

It is suggested that the cutaneous reactions attributed to atabrine should be grouped under the heading "atabrine dermatitis complex" and be classified as: (*a*) lichenoid dermatitis; (*b*) lichenoid and eczematoid dermatitis; (*c*) eczematoid dermatitis; (*d*) exfoliative dermatitis secondary to (*a*), (*b*) or (*c*).

Usually the disease is characterized by localized violaceous or erythematous eczematoid plaques on the dorsal surface of hands or feet, side of the neck, or elsewhere, followed by generalization of the lesions with subsequent appearance of lichenoid plaques and mucous membrane lesions. A characteristic eczematoid dermatitis has also occurred in persons taking suppressive atabrine. There are bilateral, symmetrical, violaceous-tinged, vesicular, eczematoid and oozing plaques on hands, feet, legs and sometimes other parts of the body. Secondary pyogenic infection is common.

The treatment of these conditions depends on early recognition of their nature and discontinuation of atabrine. Whenever possible such cases should be seen by a competent dermatologist and every effort should be made to rule out other aetiological factors. The very much higher incidence in New Guinea and adjacent islands, Assam and North Burma than elsewhere suggests that climatic or other geographical factors play a rôle in causation. Various forms of cutaneous trauma may contribute to the onset and localization of lesions.

An adequate summary of this important paper is not possible. The general statement at the end of the report, "for the information and guidance of all concerned," is as follows:—

"(1) The military value of atabrine in suppressing vivax malaria and curing falciparum malaria far outweighs untoward effects which have been attributed with reason to the use of the drug.

"(2) Suppressive doses of atabrine greater than 0·7 gm. per week should not be employed routinely. This amount has been shown to provide adequate protection against clinical attacks of malaria, provided atabrine discipline is strictly enforced. In clinical treatment of malarial attacks with atabrine, routine dosage should not exceed 2·8 gm. in seven days.

"(3) Atabrine suppressive medication should be discontinued promptly and atabrine should not be given for clinical treatment when persons develop atypical lichen planus, unexplained chronic eczematoid dermatoses, unexplained toxic erythematous eruptions, exfoliative dermatitis, severe leukopenia, agranulocytosis and aplastic anemia, acute hepatitis (not including disturbances believed to be due to malaria) or toxic psychoses which can be reasonably attributed to atabrine after careful clinical study.

"(4) It should be remembered that drugs other than atabrine, such as the sulfonamides and arsenicals, may be harmful to persons with the conditions mentioned.

"(5) Caution should be exercised in attributing disease conditions to atabrine until careful and complete studies have been made over a period of time to establish such relationship. Because of the widespread use of atabrine, its administration inevitably coincides with many diseases with which the drug has no connection. Even if a connection is established between atabrine and a given untoward effect, its significance relative to the military value of atabrine requires evaluation. It should be remembered that, since the use of atabrine became widespread, clinical attacks of falciparum malaria have been almost eliminated and deaths from

malaria have been extremely rare. There is no question of the general superiority of atabrine over quinine, both for suppression and for clinical treatment."

Norman White.

WHITEHILL, R. **Skin Sensitivity due to Atabrine.** *Bull. U.S. Army Med. Dept.* 1945, Dec., v. 4, No. 6, 724–5.

An Army nurse had occasional contact with atabrine [mepacrine] during 1939, 1940 and 1941, and from October 1942 she had frequent contact with it every day. She was admitted to hospital on 6th November, 1943, with an itching rash on the eyelids. There was no family or personal history of allergy or of skin disease. She had used various cosmetics and a hair lotion for dandruff. The rash appeared 3½ weeks before her admission as a small scaly lesion on the lids of the right eye, on the left eyelids next day, and a few days later a small patch appeared behind the right ear. The patches slowly enlarged and the itching interfered with sleep.

On admission the skin of the eyelids and behind the right ear showed a scaly erythematous rash and the conjunctivae were somewhat injected. Patch tests with the cosmetics and other substances with which she had had contact gave negative results. She was treated with Burow's solution [Liquor Aluminii Acetas] diluted 1 : 20 and on November 20th she returned to duty in the medical ward.

On 24th November the rash reappeared on her eyelids as an erythema with tiny vesicles. Patch tests were made with various drugs and all were negative except the test with atabrine, which produced a 3+ reaction with erythema and a few vesicles, itching beginning within 12 hours. The rash gradually faded and disappeared in two weeks. The nurse was transferred to a surgical ward and had no further attacks. *J. F. Corson.*

NELSON, L. M. **Dermatitis from Atabrine.** *Bull. U.S. Army Med. Dept.* 1945, Dec., v. 4, No. 6, 725–7.

Two cases of dermatitis in American soldiers, apparently caused by atabrine, are reported. The first patient developed a pruritic dermatitis about 2 months after he began to take suppressive doses (0·4 gm. a week in divided doses) of atabrine in the summer of 1943; the rash appeared first on his wrists and afterwards in spots all over his body. When he stopped taking atabrine in the autumn of 1943 the rash disappeared but returned in the following May, 11 days after he again began to take atabrine. He was now seen by the author who observed that he had violaceous macular lesions about 5 mm. in diameter on the front of his wrists and upper part of the palms of his hands. He stopped taking atabrine and the pruritus disappeared in 3 days. For diagnostic purposes he again took 0·1 gm. of atabrine on June 2, 3 and 4 and the same pruritic rash reappeared on June 4. A patch test of atabrine applied on June 5 was negative on June 7.

The second patient took atabrine in suppressive doses (0·4 gm. a week in divided doses) during the summer of 1943 until his admission to hospital on October 15. In the last week of September he developed dermatitis on the left ankle and right wrist; this was treated with sulphadiazine ointment but the rash appeared on the eyelids and ears and, after admission, bullae appeared on the arms and legs and a generalized exfoliative dermatitis finally developed. He lost part of his hair and deep depressions formed on the finger nails. He slowly recovered under local treatment in hospital and was discharged on 5th February, 1944.

He had minor local attacks of dermatitis between February and April and on April 14 he again began to take atabrine as before; three days later his

eyes and ears became swollen and he was admitted to hospital and was seen by the author. He then had generalized dermatitis—exudative on the groins, genitalia, popliteal and cubital spaces and ears, oedema of the face, especially the eyelids, follicular vesicles on the arms and thighs, and vesiculo-papules over the rest of the body. He gradually recovered under local treatment.

A patch test of atabrine was negative at 48 hours and positive (papulo-vesicular rash) at 60 hours ; a patch test with 5 per cent. sulphadiazine in lanoline and petrolatum was positive (vesicles) at 48 hours, while a patch test with powdered quinine was negative at 48 hours. A patch test with atabrine done on 8 control persons was negative.

Few cases of dermatitis due to atabrine have been reported ; the author saw another case, in a medical officer, in 1943, and refers to two cases reported by Noojin and Callaway (*North Carolina Med. J.*, 1942, v. 3, 239).

J. F. Corson.

Chopra, R. N. & Chopra, I. C. **Individual Variations in the Absorption of Drugs from the Gastro-Intestinal Tract.** *Indian Med. Gaz.* 1945, May, v. 80, No. 5, 267–71.

A description of the physiology of the various parts of the alimentary tract precedes a discussion of the factors responsible for remarkable individual variations observed in the absorption of drugs, not least of antimalarial drugs. The absorption of drugs is modified in inflammatory conditions of the mucous membrane of the gut, and by hypoacidity which commonly characterizes chronic dysentery and other infections. The rapid passage of meals through the intestinal tract, in dysenteries, liver diseases and other conditions, hinders absorption. Five illustrative cases are described in which failure of malaria infected patients to respond to the administration of antimalarial drugs was explained by much delayed absorption, as revealed by urine examination.

Norman White.

Boyd, M. F. & Kitchen, S. F. **On the Employment of Quinacrine Hydrochloride in the Prevention of Malaria Infections.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 307–14.

The experiments described were designed to assess the protection afforded by mepacrine against malaria infection. Patients were inoculated by the application of various lots of insectary-reared *A. quadrimaculatus* experimentally infected with either *P. vivax* or *P. falciparum*. The patients were white adult males, presumably susceptible to infection. The experiments, which are described in detail, indicate that the administration of mepacrine, 0·1 gm. six days a week, begun a week before and continued throughout the period of exposure, gave complete protection against *P. falciparum*, but failed to protect against *P. vivax*. In some instances the small dose of 0·1 gm. on two discontinuous days a week appeared to protect against *P. falciparum*, and in one case, though parasites appeared in the blood, there was no clinical malaria. Even if the period of administration of 0·1 gm. six times a week be commenced two weeks before and continued to two weeks after the period of exposure to infection, *P. vivax* later becomes clinically active, after protracted incubation periods.

Norman White.

Lewis, R. A. & Kibbe, F. W. **Suppression as an Adjunct to the Therapy of Malaria in Non-Malarial Areas.** *Bull. Johns Hopkins Hosp.* 1945, Sept., v. 77, No. 3, 211–17.

These observations concern a group of 63 members of the Medical Detachment of a General Hospital, who were suffering from *P. vivax* infections causing

frequent early relapses. The observations were made in an area in which there was no possibility of natural reinfection. The clinical treatment of the acute attack most frequently employed was 2·8 gm. of atabrine during a seven-day period. It was found that if the clinical treatment of the recurrence was followed by the administration of 0·1 gm. atabrine daily for two months, the interval between relapses was increased from less than six weeks to more than four months, and the percentage of relapses was reduced from 80 to less than 50. The less frequent periods of hospitalization resulting from this suppressive treatment resulted in improved morale. Many of the men so treated gained weight, notably so in the case of men in whom repeated attacks of malaria and weight loss had been associated. In most cases headache and weakness cleared up, but there were exceptions. *Norman White.*

BUXTON, P. A. **Experiments with DDT in Solutions and Emulsions against Mosquito Larvae in West Africa.** *Bull. Entom. Res.* 1945, Sept., v. 36, Pt. 2, 165–75.

The experiments described were carried out near Takoradi, Gold Coast, and were designed to assess the relative effectiveness of different preparations containing DDT as larvicides. These were tested against *A. funestus* larvae in ditches, about two feet wide, separated from each other by ridges some six feet wide, in a vegetable garden; these provided good opportunities for repetition and measurement of dose of larvicide per unit area.

An emulsion was made by dissolving DDT in two volumes of lubricating oil (Pool Grade 3) and one volume of Amoa A.S.X., an oil-soluble emulsifier: the DDT content was 5 per cent. by weight of pure DDT. Diluted to 1 : 10 this makes a very lasting emulsion.

A dieseline solution was made by dissolving a commercial DDT, 60 per cent. pure, in a locally available dieseline: generally a 5 per cent. concentration of pure DDT was used, but for putting on very small doses a 0·5 per cent. concentration was suitable.

Preliminary experiments showed that neither kerosene nor dieseline without DDT were larvicidal in doses up to 0·5 cc. per square yard.

The dieseline solution was more effective than the emulsion, as is shown in the following table :—

Dose cc. 5 per cent. pure DDT per sq. yd.	Emulsion		Dieseline	
	Immediate (kill %)	Lasting (days)	Immediate (kill %)	Lasting (days)
0·01	—	—	100	1–2
0·02	Nil	Nil	80–100	2–3
0·10	Over 80	1–2	100	4
0·50	95–100	7–10	100	5 (several weeks partial)

In shallow water DDT seems to dissolve from oil into water so as to make a larvicidal solution.

The larvicidal effect passes off in a few days even when a high dose (0·10 cc. of 5 per cent. DDT per square yard) has been applied on stagnant water. It is not known what happens to the DDT. A heavy dose (0·5 cc.), after a period of complete kill, exercises partial irregular larvicidal effect for as much as four weeks; this action is not explained.

Creatures that prey on mosquito larvae were not destroyed in these experiments. *Norman White.*

CAMBOURNAC, F. J. C. & SIMÕES, J. M. P. Nota sôbre alguns ensaios realizados com Neocid e 7013 Geigy contra as larvas de *Anopheles.* [**Experiments with Neocid and 7013 Geigy as *Anopheles* Larvicides.**] *An. Inst. Med. Trop.* Lisbon. 1944, Dec., v. 1, No. 2, 383–92.

Neocid and 7013 are substances allied to DDT (dichlor-diphenyl-trichlor-ethane). Neocid is said to have the composition trichlor-4, 4-dichlor-diphenylmethane, mixed with an inert powder in the proportion of 5 per cent. The composition of 7013 Geigy is not given. The larvicidal action of both these substances was tested against the larvae of *A. maculipennis atroparvus* under natural conditions. They were applied as 1 per cent. mixtures with road dust and in liquid suspension. The amounts of Neocid in suspension were 0·05 gm. and 0·2 gm. per square metre, and with dust 0·1 gm. per square metre. The amounts of 7013 used were 0·2 gm. per square metre in suspensions and 0·1 gm. per square metre in dust. On occasion larvae were totally eliminated, but the results were not consistent. Sometimes the smallest larvae appeared most resistant ; at other times larvae of the later stages. The larvicidal action was of short duration. *Norman White.*

WHITE, R. Senior, **House Spraying with D.D.T. and with Pyrethrum Extract compared : First Results.** *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 83–93.

The locality selected for this experiment is in the hyperendemic Jeypore Hills; the malaria conditions in this area have been previously described by the author [this *Bulletin,* 1937, v. 34, 627]. The three villages referred to in this paper still have very high spleen rates, Chatikona 98·0, Jimidiguda 87·8 and Bariguda 92·7 per cent. Jimidiguda, a small village of 48 houses, was sprayed with a 5 per cent. solution of DDT in grade III kerosene, applied with a De Vilbiss paint gun served by a Kapur hand pressure sprayer, at the rate of 1 qt. per 1,000 square feet of wall surface. Care was taken to wet all the wall surfaces including outside verandahs, and the roofs as far as accessible. Chatikona was sprayed with pyrethrum insecticide. Bariguda was an untreated control. The author's conclusions are as follows :—

" (i) D.D.T. at the rate of 1 qt. 5 per cent. solution per 1,000 sq. ft. will prevent infection in the *fluviatilis*-group in a hyperendemic area, in the ' cold ' weather of Southern India, for eight weeks. It acts by reducing density as well as longevity.

" (ii) Pyrethrum spraying, 6 days each week, reduces density and longevity sufficiently to inhibit gland infections. The density reduction is much less than with D.D.T. This is probably due to a certain proportion of the house population leaving before the morning pyrethrum spraying, whereas with D.D.T. it is believed that any specimen which has rested after feeding on a still active treated surface must die.

" (iii) Pyrethrum spraying twice a week . . . has no effective result either on density or on infectivity. As a method of protecting a population exposed to the *fluviatilis*-group it is useless. . . .

" (iv) Assuming the cost of D.D.T. as stated to be correct [Rs. 3 per lb.], over the two months December to February, a period of heavy though not of maximal transmission, D.D.T. is 20 to 25 times cheaper per capita per week than pyrethrum."

Norman White.

COLLIGNON, E. La campagne antipaludique de 1944 dans le département d'Alger. [**The Antimalaria Campaign in the Department of Algiers in 1944.**] *Arch. Inst. Pasteur d'Algérie.* 1945, June, v. 23, No. 2, 98–110.

As in 1943, the malaria campaign in 1944 concentrated on the protection of military forces stationed in the Algiers Department. The antimalaria services of the British and United States armies, and of the local government, were each responsible for a delimited area. This arrangement only related to measures against the anopheline vector, drug prophylaxis being in the charge of each authority as concerned its own personnel.

It was a difficult year for the departmental service. The shortage of antimalarial drugs prevented their use for prophylaxis. Transport difficulties and the difficulty of recruiting labour of a reliable type were obstacles to the satisfactory execution of antilarval measures. Nevertheless, the malarial situation was not unsatisfactory, there were no important epidemic manifestations, and climatic conditions limited anopheline breeding places. Indices of infection were, if anything, somewhat lower than in the two preceding years.

Norman White.

VINCKE, I. with PARENT, M. Un essai de lutte antimalarienne spécifique à Stanleyville. [**Control of Malaria in Stanleyville by Species Sanitation.**] Reprinted from *Bull. Ass. des Ingénieurs de la Faculté Technique du Hainaut, à Mons.* 1944, Oct., No. 8, 23 pp., 7 graphs & 1 map. [15 refs.]

Anopheles gambiae is by far the most important vector of malaria in Stanleyville and from 1935 to 1940 all efforts were concentrated on the control of this species. This paper describes the results achieved. *A. moucheti*, *A. nili* and *A. funestus* are also vectors of malaria but their relative infrequency makes them comparatively unimportant. Thus, of more than 50,000 identified anophelines captured in dwellings, *A. gambiae* formed 85·5 per cent., *A. nili* 8·7, *A. moucheti* 5·6, and *A. funestus* 0·18 per cent. Of 18,396 anopheline breeding places, 93·5 per cent. harboured larvae of *A. gambiae*. Temporary breeding places of *A. gambiae* have necessitated close and constant supervision ; oiling or filling was used in their treatment. Permanent breeding places have necessitated drainage works. Creeks and inlets from rivers have presented great difficulties ; some success has been achieved by providing shade for breeding places with a species of Cassia, *C. alata*, which flourishes in damp situations.

In 1938, oiling which previously had been done at 10-day intervals was carried out weekly ; thereafter there was a marked diminution in the anopheline infestation of houses. But the improvement was not reflected in any diminution in the parasite rate of children between 5 and 10 years of age ; this rate was 95·7 in 1940. The spleen rates of children of the same age were much lower than those reported for Stanleyville by SCHWETZ in 1931 ; he reported a rate of 94·8 as compared with 37 in 1940, but the fall preceded the antilarval work reported in this paper.

Of the positive blood slides from children aged 5 to 10, *P. falciparum* was found in 94·5 per cent., *P. malariae* in 22 per cent. and *P. vivax* in 4·5 per cent.

Anopheles dissected numbered 36,826. The sporozoite index of 30,780 *A. gambiae* was 6·49, of 3,589 *A. nili* 4·3, of 2,082 *A. moucheti* 4·4, and of 375 *A. funestus* 6·6.

Norman White.

REV. PALUDISME ET MÉD. TROP. 1945, Dec. 15, v. 3, No. 21, 167–76. La lutte contre le paludisme dans la France d'Outre-Mer. [**Malaria Control in French Overseas Territories.**]

FELTON, H. L., BARNES, R. C. & WILSON, A. **Malaria Control in a Non-endemic Area.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 201–8. [16 refs.]

The return of service personnel and the introduction of prisoners of war from many parts of the world, infected with malaria, involves risks not limited to those parts of the United States in which malaria is endemic at the present time. This paper describes the activities of a sub-office of "Malaria Control in War Areas," with headquarters in New York, that is responsible, in collaboration with local authorities, for the execution of preventive measures around military installations in the New England States, New York, New Jersey, Pennsylvania and Delaware. Mobile malaria control units have been established at strategic places. Each unit consists of a station wagon and a 1½-ton truck which carries material for entomological surveys and inspections, larvicidal operations, minor drainage, clearing and cleaning, and spray-killing adult mosquitoes: an engineer or entomologist is in charge and is accompanied by the necessary semi-skilled assistants. Surveys are made around concentrations of prisoners of war and service personnel, and assistance is given to local agencies making such surveys in non-military areas. Mosquito control measures are carried out wherever human carriers and the mosquito vector are concentrated. In addition, demonstrations have been given to district and local public health officials, and laboratory workers have been trained in the recognition of malaria parasites in thick films.

During 1943 and 1944, 57 areas were surveyed in all of these north-eastern States except Vermont. *A. quadrimaculatus* was present in 32 of these 57 areas; adults were found in all the States except New Hampshire, where, however, larvae of this species were taken. In nine localities *A. quadrimaculatus* densities were high. Maximum *A. quadrimaculatus* counts for single catching-station inspections were as high as 500 in Rhode Island, 325 in Delaware, 200 in Massachusetts, 150 in New Jersey and 100 in New York. It would seem that high densities of *A. quadrimaculatus* may be found in all of the north-eastern States except Maine, Vermont and New Hampshire.

Norman White.

KIKER, C. C. & SPARKMAN, R. E. **A Review of Equipment used in applying Malaria Control Measures on Impounded Waters in the Tennessee Valley.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 209–22, 9 figs.

This is a brief description of machines and equipment of many kinds that have been used in the comprehensive programme of malaria control of the Tennessee Valley Authority during all stages of construction of impounded waters. Tractor-drawn and self-propelled machines used for clearing the land to be submerged and for shore-line maintenance, a floating underwater weed cutter, and two types of spray equipment for applying insecticidal sprays are among the equipment described in a paper which does not lend itself to summary. *Norman White.*

KRUSE, C. W. & GARTRELL, F. E. **The Use of House Mosquito-Proofing as an Emergency Malaria Control Measure in the Kentucky Reservoir.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, June, v. 4, No. 2, 133–46, 2 figs.

PARAENSE, L. Aspectos parasitários observados no local inoculado com esporozoitos de *Plasmodium gallinaceum*. (Nota preliminar.) [**Parasitic Aspects observed at the Site of Inoculation with *P. gallinaceum* Sporozoites.**] *Mem. Inst. Oswaldo Cruz.* 1943, June, v. 38, No. 3, 353–9, 1 coloured pl. English summary.

The paper reports the results of an investigation into the development of sporozoites of *P. gallinaceum* when injected by mosquito bite or by syringe into the skin of chicks. The skin at the site of injection was removed at varying intervals and pinned out on a board, with the subcutaneous surface uppermost. Scrapings were then made of the dermis, and with the material thus obtained films were made. These were stained with Giemsa stain and searched for possible developmental forms of the malarial parasite. Films made from skin 6 to 12 hours after injection showed many elongate bodies with eight or more chromatin granules. They were considered to be evolutionary forms of sporozoites. At the 18, 24, 60 and 84-hour periods the films showed small intracellular oval bodies with one or two chromatin masses. After the 84-hour period parasites appear in the blood, following which, after 1, 24 and 48 hours, smears from the injection sites reveal numerous exo-erythrocytic schizonts within large cells. The paper is illustrated by a coloured plate depicting some of the developmental forms encountered.

C. M. Wenyon.

SEELER, A. O., MALANGA, C. & PIERSON, J. **Effect of Streptomycin on Avian Malaria.** *Proc. Soc. Exper. Biol. & Med.* 1945, June, v. 59, No. 2, 291–2.

The authors have tested the action of streptomycin on three species of avian malarial parasite (*P. cathemerium*, *P. lophurae* and *P. gallinaceum*) in Leghorn chicks. The infections were produced by intravenous inoculation of infected blood, and, in the case of *P. gallinaceum*, of sporozoites also. Treatment was commenced within an hour of inoculation, by intramuscular injection of the antibiotic every three hours during five days (three days in the case of the sporozoite-induced infection). The birds were in groups of five, and the dose for each group varied from 25,000 to 400,000 units per kilogram of body weight per day. The effect of the drug, if any, was estimated by parasite counts made on the fifth day (ninth day in the sporozoite-infected birds). In the blood-inoculated birds the infections developed as in the controls, but in those inoculated with sporozoites the percentage of infected cells in the blood varied from 40·8 to 17·7, according as the doses of streptomycin varied as indicated above. In 10 control chicks the percentage of infected cells was 35·1. The results indicate that streptomycin has no suppressive action on the blood-inoculated infections but has a slight action on those induced by sporozoite inoculation.

C. M. Wenyon.

ROSTORFER, H. H. & RIGDON, R. H. **Anoxia in Malaria. An Experimental Study on Ducks.** *J. Lab. & Clin. Med.* 1945, Oct., v. 30, No. 10, 860–66, 4 figs.

In previous papers the second author has shown reason for supposing that anoxia plays an important part in deaths from *P. falciparum*, *P. knowlesi* and *P. lophurae* infections [this *Bulletin*, 1943, v. 40, 118 and 436; 1945, v. 42, 540]. Recently, with VARNADAE (*Amer. J. Trop. Med.*, to be published), he has shown that transfusion of red cells will prolong the course of the infection in ducks but will not prevent ultimate death. In the present paper an account is given of experiments in which chicks and ducks infected with *P. lophurae* were exposed to reduced oxygen tension. This was accomplished by keeping

them in a special chamber in which atmospheric pressure could be reduced to represent the conditions of altitudes up to 20,000 feet. The rate of " ascent " was 1,600 feet per minute during the first 12 minutes, followed by 600 feet per minute. It was found that both normal and infected chicks and ducks succumbed to the reduced oxygen tension, but that the infected birds did so before the normal birds. The normal birds developed a polycythaemia of 4 million red cells in comparison with a normal of 2·5 million. In ducks this level was reached in three days.

In another experiment a comparison was made of four infected ducks kept at normal atmospheric pressure and four at the reduced pressure of 20,000 feet. The total red cell count showed an increase on the second day, and a subsequent fall, in both groups. The fall is, however, more rapid in the normal-atmosphere group, while the total number of parasitized cells is one-third greater in the reduced-pressure group. The total number of unparasitized cells decreases rapidly in both groups so that, ultimately, the complete loss of these cells seems evident. The formation of young cells is more rapid in birds kept at high altitude. The increase in number of the new cells does not prevent the rapid disappearance of the old cells. The rate of disappearance of adult cells is the same in both groups, though the total parasite count is higher in the reduced-atmosphere group. Observations were also carried out on six ducks, two of which were kept at normal atmospheric pressure and four at reduced pressure. Of the four, two were removed from the chamber after five days. The results were very much the same as in the previous experiment. Of the two removed after five days, one recovered and its rate of recovery was approximately the same as that of one of the two kept at a normal pressure, which also recovered.

The experiments indicate that birds with a mild infection do not tolerate severe anoxia such as occurs at high altitudes. They first show the effects of anaemic anoxia before the infection has reached the stage at which malarial symptoms would become evident. The symptoms of anoxia in infected and uninfected birds are the same, with the difference that they appear at a lower altitude and after a shorter exposure in the former group. It appears that the decrease in resistance to anoxia in infected birds is the result of the failure of the oxygen transporting system to meet reduced oxygen pressure. The high total parasite count in infected birds at high altitudes is a result of the induced polycythaemia and the greater opportunity the parasites have of infecting red cells.

The authors conclude that the data presented in their paper lend support to the view that anoxia plays an important rôle in the mechanism of death from acute malarial infections. *C. M. Wenyon.*

Rigdon, R. H. & Rudisell, H., Jr. **Effect of Radiation on Malaria. An Experimental Study in the Chick and Duck.** *Proc. Soc. Exper. Biol. & Med.* 1945, June, v. 59, No. 2, 167–70, 2 figs.

One of the authors (H. R.) having shown that splenomegaly resulting from chronic malaria was reduced, with corresponding improvement in health, by treatment with Roentgen irradiation, it was considered of interest to investigate the effect of irradiation on more easily controlled malarial infections. Those of *P. lophurae* in chicks and ducks were selected. In the first place citrated infected blood was exposed in Petri dishes to varying amounts of irradiation, and was then inoculated intravenously to chicks and ducks. It was found that the intensity of infection produced in a given time decreased with the amount of irradiation till finally an amount was reached which rendered the blood entirely non-infective. When infected chicks were exposed to the rays there was a reduction in the intensity of the infection, the greatest reduction being in the

chicks which had been exposed to the greatest amount of irradiation. The effect of radium bromide was tested by mixing a solution of this substance with citrated infected blood in Petri dishes, or by inoculating the solution intravenously to infected chicks and ducks. In neither case was there evidence of any lethal action of the drug on the parasites, though in the case of the *in vivo* test the amount administered was sufficient to cause severe tissue degeneration. In the Roentgen ray experiments, as the amount of irradiation needed to bring about a significant reduction of the infection was very near the dose lethal for the chicks and ducks, it would seem that this type of therapy for malaria would be impracticable unless other malarial parasites proved much more susceptible. Similar experiments with *P. gallinaceum* have been described by Bennison and Coatney [this *Bulletin*, 1945, v. 42, 623]. *C. M. Wenyon.*

i. Freund, J., Sommer, Harriet E. & Walter, Annabel W. **Immunization against Malaria : Vaccination of Ducks with Killed Parasites incorporated with Adjuvants.** *Science*. 1945, Aug. 24, 200–202.

ii. ——, Thomson, K. J., Sommer, Harriet E., Walter, Annabel W. & Schenkein, Edna L. **Immunization of Rhesus Monkeys against Malarial Infection** (*P. knowlesi*) **with Killed Parasites and Adjuvants.** *Ibid.* 202–4. [Refs. in footnotes.]

Experiments by various observers have shown that antibody production against certain antigens is increased and made to last longer if the antigens injected are combined with a lanoline-like substance (Falba) and paraffin oil with or without killed tubercle bacilli [see *Bulletin of Hygiene*, 1945, v. 20, 585]. In the papers under review experiments are described in which this procedure was applied in attempts to immunize young ducks against *Plasmodium lophurae* and *rhesus* monkeys against *P. knowlesi*, both of which usually produce fatal infections.

i. In the first paper the experiments with ducks are considered. Heavily parasitized red cells were suspended in salt solution containing 0·1 per cent. formaldehyde and kept at a temperature of 4°C. overnight. The cells were then washed three times with saline and mixed with Falba and paraffin oil. The ducks to be protected received two injections of this mixture together with killed tubercle bacilli and one injection of the mixture without tubercle bacilli, a period of one month intervening between the injections. A month after the last injection of antigen, in each of two experiments, four immunized and four control ducks received approximately one billion parasites intravenously. The blood examinations carried out clearly indicated that the intensity of infection in the immunized ducks was very much lower than in the controls. Thus in the first experiment none of the immunized ducks showed more than an average of 7·6 parasites per 100 red cells, while none of the controls showed less than 54. Two of the controls died from their malaria infection. One of the immunized ducks also died, the cause of death being generalized peritonitis. It is clear that the immunized ducks had acquired a considerable resistance to subsequent infection with *P. lophurae*.

ii. In the second paper are discussed similar experiments with *rhesus* monkeys and *Plasmodium knowlesi*. The antigen was prepared from heavily infected blood as described above and monkeys received two or three subcutaneous injections of this antigen with killed tubercle bacilli. When injected intravenously with infected blood 14 control monkeys rapidly became infected. Of these four died of malaria ; nine, most if not all of which would have died, were killed in order to recover parasites for vaccine production, while one survived. Of similarly treated immunized monkeys one failed to show parasites at any time in thin smears, while 6 developed infections of 1 to 10 parasites per 100

red cells. These subsequently disappeared. It is concluded that the method of immunization modifies parasitaemia and prevents fatal infection with *P. knowlesi* in *rhesus* monkeys. *C. M. Wenyon.*

TRYPANOSOMIASIS.

CAUBET, P. Différences morphologiques chez deux souches de *Trypanosoma gambiense* déterminant des maladies expérimentales différentes. [**Morphological Differences between Two Strains of *Trypanosoma gambiense* causing Different Experimental Infections.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 9/10, 285–90, 2 figs. [15 refs.]

The author measured the trypanosomes of two laboratory strains of *Trypanosoma gambiense*, using stained thin blood films and a camera lucida. One strain, called the Antwerp strain, produced acute infections in mice and rats, while the other, called the Yaunde strain [Cameroons] caused chronic and irregular infections and sometimes produced paralysis in mice; the latter strain has been the subject of previous observations [see ROUBAUD & PROVOST, this *Bulletin*, 1939, v. 36, 746; 1942, v. 39, 234; STÉFANOPOULO & ETÉVÉ, *ibid.*, 1945, v. 42, 258].

The measurements of the two strains are shown in tables and curves. The trypanosomes of the Antwerp strain were, in general, shorter than those of the Yaunde strain, owing chiefly to differences in the length of the free flagellum; in the Antwerp strain the total length of the trypanosomes varied from 18 to 30μ (average 24·5μ) in the guineapig and from 16 to 28μ (average 22·9μ) in the rat, while the corresponding figures for the Yaunde strain were 20 to 34μ (average 29μ) and 20 to 34μ (average 27·8μ).

These differences between the two strains were maintained through many passages in animals during six months and the strains could readily be distinguished in thin blood films on simple microscopic examination.

In accordance with the views of LAVIER [this *Bulletin*, 1944, v. 41, 368], the author thinks that the morphological differences may be associated with differences in the rates of multiplication of the trypanosomes, the longest ("oldest") forms tending to be eliminated among the rapidly dividing trypanosomes of the Antwerp strain. *J. F. Corson.*

JACKSON, C. H. N. **Comparative Studies of the Habitat Requirements of Tsetse Fly Species.** *J. Animal Ecology.* 1945, May, v. 14, No. 1, 46–51.

In an attempt to discover why different species of *Glossina* are found in different types of country, *G. morsitans* and *G. palpalis* were introduced into territory where *G. swynnertoni* normally occurs. This was done by allowing pupae, brought from indigenous areas, to hatch in the new habitat.

The *morsitans* were able to produce a second generation in the new environment, but were physiologically inferior to *morsitans* in a normal habitat, being smaller and containing less reserve fat. It is suggested, however, that this species would die out, not so much for physiological reasons, but because the predominant *swynnertoni* males would impregnate the *morsitans* females; such females are either barren or produce few, mostly sterile, offspring.

G. palpalis did not produce a second generation under the new conditions, although a seasonal stream (containing water at the time of the experiment) was in the vicinity.

Laboratory experiments to elucidate these results are described, and future work is suggested. The ability of each species to colonize a particular type of

country appears to be related more to its behaviour (frequency of feeding, choice of resting place) than to its straightforward physiological reactions to climatic conditions. *Kenneth Mellanby.*

GASCHEN, H. La répartition des tsétsés en fonction du climat. [**The Distribution of Tsetse Flies in relation to Climate.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 5/6, 172–5.

——. L'utilité du climogramme pour l'étude de la biologie des tsétsés. [**The "Climogram" in the Study of Biology of Tsetse Flies.**] *Ibid.*, 176–80, 1 fig.

Details are given of how the limiting conditions of temperature and humidity, under which *Glossina tachinoides*, *G. morsitans* and *G. palpalis* occur, can be determined and expressed graphically; and the way in which these climatic conditions are related to other factors such as vegetation, in the ecology of the tsetse, is discussed. The "ideal" climatic zone for *G. tachinoides* is very much larger than that for *G. palpalis*, which is much more susceptible to adverse conditions such as high temperature and low relative humidity. *G. morsitans* is intermediate between the other species in the range of its climatic requirements. *K. Mellanby.*

GASCHEN, H. Variations saisonnières des tsétsés. [**Seasonal Variations of Tsetse Flies.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 7/8, 250–53, 2 figs.

The relative abundance of *Glossina palpalis* and *G. tachinoides* at different seasons of the year is related to the changes in the temperature and humidity at the different seasons. The author considers that there is a close correlation between the abundance of *G. palpalis* and the moisture of the air; from March to June, when the relative humidity is rising from 40 to 80 per cent., the fly-population increases greatly. Later in the year the fly catches are smaller, owing to the wide dispersal of the flies from their dry weather foci. With the return of hot dry weather the flies are reduced in numbers and the extent over which the species can range is also restricted. *G. tachinoides*, being much less susceptible to desiccation, is less closely dependent on a favourable atmospheric humidity, and variations in the density of *G. tachinoides* population are not correlated in the same way. *Kenneth Mellanby.*

NEEL, R. Sur un cas de trypanosomiase africaine au début, avec complications rénales, observé chez un Européen au Soudan. [**An Early Case of Sleeping Sickness with Renal Complications, in a European.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 3/4, 100–107, 3 figs.

LWOFF, M., Mme., BOVET, D. & FUNKE, A. Activité *in vitro* sur les trypanosomidés de quelques dérivés de l'éthylène diamine. [**Action of various Derivatives of Ethylenediamine on Trypanosomidae** *in vitro*.] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 7/8, 229–36.

It had previously been shown that a number of derivatives of ethylenediamine possess therapeutic properties against *T. brucei* infections in mice (FUNKE, BOVET and MONTEZIN, this *Bulletin*, 1944, v. 41, 734). These were of the types :—

(I) $R.C_6H_4.CH_2NH\ (CH_2)_2NH_2$, and
(II) $R'C_6H_4.CH_2.NH\ (CH_2)_2NH.CH_2.C_6H_4.R'$,

where R and R' are various hydrocarbon radicles. The present studies are intended to show whether such compounds exhibit any activity against artificial cultures of flagellates. The organism chosen for the tests was *Strigomonas*

oncopelti, a non-pathogenic parasite of Hemiptera and plants, a peptone-saline culture medium being used, adjusted to *p*H 7·0. One compound was tested also against *Leishmania tropica, L. donovani* and *Trypanosoma cruzi* in a semi-solid blood-containing culture medium. The experiments were conducted at 26–28°C., in drug-concentrations of 1/1,000, 1/2,000, 1/5,000 and 1/10,000.

Eighteen compounds were tested, results being presented in a Table. The authors' conclusions are that the degree of correspondence between the findings *in vitro* and those previously obtained *in vivo* varied in different chemical groups, as follows :—

(*a*) Monosubstituted derivatives of ethylenediamine showed a very close correspondence of activity *in vitro* and *in vivo*. For example, considerable activity was shown both *in vitro* and *in vivo* where R=C_5H_8, *i.e.* N-*p*-*cyclo*-pentylbenzylethylenediamine, and where R=C_3H_7, *i.e.* N-*p*-*n*-propylbenzyl-ethylenediamine and N-*p*-*iso*propylbenzylethylenediamine. The latter compound was the only one tested also against *Leishmania tropica, L. donovani* and *T. cruzi*, and a degree of activity *in vitro* was demonstrated against these organisms similar to that displayed against *Strigomonas oncopelti*. Methylation of the benzene ring in the last-named compound apparently resulted in no great loss of activity *in vitro* or *in vivo*, but introduction of an amino group on the ring led to considerable loss of activity under both these experimental conditions. Other compounds inactive *in vitro* and *in vivo* were the unsubstituted member (R=H), and that in which an amino group occupied the position of R.

(*b*) There was also close correspondence between results *in vitro* and *in vivo* with several compounds of types similar to those above, but containing a naphthalene instead of a benzene ring. Thus N-(1-naphthylmethyl)-ethylenediamine was only feebly active *in vitro* and *in vivo*, but substantial activity was shown under both these conditions by N-(5 : 6 : 7 : 8-tetrahydro-2-naphthylmethyl)-ethylenediamine and N-(4-*iso*propyl-1-naphthylmethyl)-ethylenediamine, as well as by the only non-aromatic diamine examined, N-citronellyl-ethylenediamine.

(*c*) Among the remaining compounds tested there was less correspondence between results *in vitro* and *in vivo*. Thus, a certain degree of activity *in vitro*, but none *in vivo*, was exhibited by the two symmetrical disubstituted compounds tested (see general formula II above), where R=H or C_3H_7 (*iso*propyl). This was also the case with two compounds in which the ethylenediamine chain was replaced respectively by 1 : 6-diaminohexane and by piperazine.

(*d*) The reverse effect, *i.e.* inactivity *in vitro* associated with substantial activity *in vivo*, was exhibited by a phenylarsonic acid substituent of ethylenediamine, *m*-ONa.OH.O : As. C_6H_1.NH. $(CH_2)_2$. NH_2. This finding is in line with the well-known property of phenylarsonic acids in general, whereby activity comes into play only after reduction by the tissues to the arsenoxide form.

E. M. Lourie.

Launoy, L. Distinction, par l'action des diamidines, entre la chimio-résistance naturelle, présentée par *T. congolense* et la chimio-résistance acquise par *T. annamense*. [**A Distinction, shown by the Action of Diamidines, between the Natural Drug Resistance of** *T. congolense* **and an Acquired Drug Resistance of** *T. annamense*.] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 1/2, 37–42.

The author compared the action of three aromatic diamidines—4 : 4′-diamidino stilbene [stilbamidine ; M. & B. 744), 4 : 4′-diamidino diphenoxypropane [propamidine ; M. & B 782], and 4 : 4′-diamidino diphenoxypentane [pentamidine ; M. & B. 800]—on two species of trypanosomes, *T. congolense*

and a strain of *T. annamense*, the latter having an acquired resistance to some compounds of antimony. The drugs were tested on these infections in mice and guineapigs.

T. congolense.—In mice, doses of 0·4 to 0·6 mgm. per 20 gm. body weight, given intravenously, caused a temporary disappearance of the trypanosomes from the peripheral blood but did not cure; in guineapigs, doses of 1 to 1·25 mgm. per 100 gm. body weight, given intraperitoneally, had little or no effect on the infection.

T. annamense.—In mice, 0·01 mgm. of stilbamidine caused a temporary disappearance of trypanosomes from the peripheral blood and 0·6 mgm. cured; 0·25 mgm. of propamidine cured some of the mice, while 0·1 mgm. of pentamidine cured some and 0·2 mgm. cured all. In guineapigs doses of 1 to 1·25 mgm. of stilbamidine or pentamidine per 100 gm. body weight caused temporary disappearance of the trypanosomes but these doses of propamidine had no effect.

The author concludes that *T. congolense*, a species with much natural resistance to drugs, and this strain of *T. annamense*, with an acquired resistance to some organic antimonials, behaved differently towards the diamidines, especially in the guineapig. [See also this *Bulletin*, 1939, v. 36, 212.]

J. F. Corson.

Goodwin, L. G. & Marshall, P. B. **The Pharmacological Properties of some Monoamidines.** *J. Pharm. & Exper. Therap.* 1945, May, v. 84, No. 1, 16–25, 5 figs. [11 refs.]

Data are reported on the toxicity, and the effects on smooth muscle, blood pressure, respiration, and c.n.s., of 36 compounds related to benzamidine. Most of the compounds showed depressor and spasmolytic activity. Several pyridyl monoamidines stimulated respiration and had considerable analeptic activity. Therapeutic tests in mouse trypanosomiasis (*T. equiperdum*, *T. cruzi*), canary malaria, and hamster leishmaniasis gave negative results.

F. C. MacIntosh.

Chen, G. & Geiling, E. M. K. **The Determination of Antitrypanosome Effect of Antimonials in Vitro.** *J. Infect. Dis.* 1945, Sept.–Oct., v. 77, No. 2, 139–43, 4 figs.

A method has been developed for the assay of trypanocidal substances *in vitro*, based on the fact that they interfere with the metabolism of glucose by the parasites, for which this substance is essential. The experiments were carried out with *T. equiperdum* which was maintained by passage in rats. The trypanosomes were isolated from the blood elements by centrifuging under standard conditions [the speed of centrifuging is given as 12 r.p.m., no doubt in error] and suspended in a medium consisting of equal volumes of rat plasma, M/15 phosphate buffer *p*H 7·4, and Ringer-Locke solution containing 0·75 per cent. glucose. Drugs were dissolved in the phosphate buffer before admixture with the other components. Over a period of 1 hour at 37°C. the rate of metabolism of glucose by the trypanosomes was constant, as estimated by the ceric sulphate microtitration method (Miller & van Slyke, *J. Biol. Chem.*, 1936, v. 114, 582). The rate and degree of inhibition of glucose metabolism by drugs at different concentrations over the same period was also estimated. The percentage inhibition was used to compare the trypanocidal potencies of different antimonials, and comparisons were based on the concentration that would give rise to a 50 per cent. inhibition. The present results obtained *in vitro* with trivalent antimonials were in good agreement with those previously

found *in vitro* by CHEN *et al.* [this *Bulletin*, 1945, v. 42, 869]. In the case of pentavalent antimonials the agreement was not so good. The present method is being applied to study the mechanism whereby these drugs exert their effects on trypanosomes. *J. D. Fulton.*

MOSELEY, V. & MILLER, H. **South American Trypanosomiasis (Chagas' Disease).** *Arch. Intern. Med.* 1945, Oct., v. 76, No. 4, 219–29, 2 figs. [Refs. in footnotes.]

Cases of Chagas's disease are not common in the Panama district; only 58 have been diagnosed in the past 15 years and only 21 have been studied clinically. For this reason, and also because the two cases here recorded differed from what is usual in adults infected and, most important, because medical men in the U.S.A., who are unacquainted with this and other tropical diseases, may meet them in returning soldiers, the authors have recorded these two carefully.

The information they give on the mode of infection, early symptoms diagnosis and clinical course is well known to all readers of this *Bulletin*, but the descriptions of the two patients, soldiers of good physique, aged 29 and 27 years respectively, are detailed because they presented the symptoms usually associated with infection in children. The symptoms and course in adults are usually of a comparatively mild character.

The first suffered also from benign tertian malaria; he presented the unusual features of generalized muscular pains and arthritis of knees and fingers. This patient made a good recovery. The second appeared in the earlier stage of his illness to be no more seriously ill than the first, but towards the third week, tachycardia and irregular arhythmia, extra-systoles and diastolic gallop rhythm, made their appearance, and from the 4th to the 18th weeks the pulse and cardiac rate and rhythm varied widely, and signs of heart block were present, which did not improve during five months' observation. The opinion held by many observers that severe myocarditis during the acute stage is limited to children clearly does not hold good. *H. Harold Scott.*

BORGES-FORTES, A. As lesões do sistema nervoso na enfermidade de Chagas (Tripanosomiase Americana). [**Lesions of the Nervous System in Chagas's Disease.**] *J. Clinicos.* Rio de Janeiro. 1945, Aug., v. 25, No. 8, 277–86. [19 refs.]

[This article is called an "original work," but is in reality a review itself and contains no statement which is not authenticated by reference to literature on the subject.] In the acute forms of nervous affection in Chagas's disease the early localization appears to be in the meninges, the brain, medulla and neuroglia, the primary site being the neuroglia cell. The leishmaniform bodies increase in number and size and form a "parasitic focus" which in time ruptures to discharge the parasites, and this leads to an acute and diffuse meningo-encephalitis. The chronic forms may be congenital, or may show themselves in childhood or adult life, with results on intelligence, speech, and motility owing to cicatricial lesions and sclerosis. Degenerative foci may arise in the cerebral cortex and in the caudate and lenticular nuclei. In certain areas, notably the globus pallidus, granulations occur which stain metachromatically and markedly with fuchsin. The inflammatory and degenerative changes in the meninges suffice to account for the psychic disturbances and focal symptoms such as aphasia, anarthria, spastic paralysis, convulsions and others. *H. Harold Scott.*

NÁJERA, L. Sobre el Tripanosoma de los lirones (*Trypanosoma blanchardi*) y de los murciélagos (*Schizotrypanum vespertilionis*) hallados en España y su interés biológico. [*T. blanchardi* **(of Mice) and** *S. vespertilionis* **(of Bats) found in Spain.**] Reprinted from *Rev. Ibérica de Parasit.* Granada. (Tomo extraordinario.) 1945, Mar., 216–45, 1 coloured pl. & 4 figs. [28 refs.]

LEISHMANIASIS.

SHORTT, H. E. **Recent Research on Kala-Azar in India.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Sept., v. 39, No. 1, 13–31. [49 refs.] Discussion 31–41 [SCOTT, H., President; TAYLOR, J.; MANSON-BAHR, P.; WHITTINGHAM, H.; LOW, G. C.; HOARE, C. A.; WENYON, C. M.; BURKE, E.; SHORTT, H. E. (in reply)].

The author divides the history of research on kala azar in India into three periods. Firstly, the one in which serious epidemics occurred in Bengal; secondly, that commencing with the discovery of the causative organism and the study of the pathology of the disease; thirdly, the recent period beginning with the discovery of effective methods of treatment and ending with the elucidation of the method of transmission. The first two periods are briefly considered but the third, a recent period in which, by his researches, the author himself played a prominent rôle, is dealt with more fully. He discusses the various methods by which experimental infections in animals can be produced, including intraperitoneal inoculation of naso-pharyngeal secretions of kala azar cases, feeding on faeces of infected animals, contact under insanitary conditions with infected animals, contamination of the conjunctiva with infected material, intraperitoneal inoculation of or feeding on sandflies which had ingested parasites. He shows how all these and other possibilities had to be considered in arriving at the natural method of transmission, which is by the bite of the sandfly. He reviews the difficulties which had to be overcome before a satisfactory method of keeping alive the infected sandflies had been devised. It was then that the final and dramatic experiment was carried out in which five volunteers were infected by the bites of sandflies previously fed on patients with kala azar.

Under the heading of treatment the author mentions the introduction by BRAHMACHARI in 1922 of urea stibamine which, in spite of the appearance of other successful organic antimonials, still remains, in India at least, the drug which is most widely used. The author thinks that it is difficult to see how any future treatment can show any marked improvement over that now available in these antimony preparations, by which cure of a disease, for which previously there was nothing to prevent a fatal termination, can be obtained sometimes in a matter of days. In considering clinical diagnosis it is pointed out that the diseases most likely to cause confusion are those of the enteric group. Spleen or liver puncture with microscopical examination of stained smears is regarded as the diagnostic method of choice for the great majority of cases. Sternal puncture is considered to be less reliable. Culture methods, xeno-diagnosis and chemical tests depending on the globulin increase in the serum are all reviewed, as also complement fixation tests, the most successful of which is based on the use of an antigen prepared from acid-fast bacilli. For prevention it is noted that the use of modern insecticides against the sandfly may give good results, while the treatment of actual cases of the disease is in itself a preventive measure, for under treatment the parasites rapidly disappear from the peripheral blood.

In the discussion which followed Col. SHORTT's paper, various questions were asked and answered, while Dr. Edmund BURKE spoke of the good results he had had in Assam in treating the disease with neostibosan and, when his supply of this was exhausted, with Glaxo Laboratories' Stibatin (sodium antimony-V-gluconate) which he considers as good as any other remedy. [Most of the information given in the paper has already been reviewed in this *Bulletin*, but its collection in a single communication by the author will be of great assistance to those who wish to follow the development of knowledge of kala azar with particular reference to India.] *C. M. Wenyon.*

BOURGAIN, M. Sur un exemplaire de *Phlebotomus papatasi* Scopoli, 1786, capturé à Toulon. [**A Specimen of *P. papatasi* captured at Toulon.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 5/6, 145–9, 1 fig.

BOURGAIN, M. Contribution à l'étude des phlébotomes du littoral méditerranéen français : présence de *Phlebotomus* (*Brumptius*) *parroti* Adler et Théodor 1926, aux Darboussèdes (Banlieue de Toulon). [**The Presence of *P. parroti* in the Toulon Area.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 5/6, 150–58, 1 fig. [17 refs.]

GOODWIN, L. G. **Oedema in Hamsters infected with *Leishmania*.** [Correspondence.] *Nature.* 1945, Oct. 20, 476.

The author has noted that Syrian hamsters infected with *Leishmania donovani* may develop severe oedema. Ascites and distension of the mesentery with fluid are the first signs. Later, gross oedema of the subcutaneous tissues develops and the skin is pulled down into a skirt around the flanks by the weight of fluid. Death occurs in a few days, following an increase in weight of as much as 50 gm. in a week. The condition appears only after several months of infection, is independent of the intensity of this infection and is not associated with any particular strain of parasite. Oedematous animals exhibit proteinuria. The kidneys are pale and enlarged and histologically reveal degeneration of the glomeruli and the presence of protein casts. It seems that the loss of protein through the kidneys is the cause of the oedema. All attempts to cultivate or demonstrate by inoculation a secondary infective agent have failed. It seems probable that the nephritis is due to a leishmanial toxin. The condition is compared with that noted by COLLIER, FULTON and INNES in mice infected with *Trypanosoma cruzi* in which, however, the kidneys were normal [this *Bulletin*, 1943, v. 40, 21]. *C. M. Wenyon.*

DASTIDAR, S. K. G. **A New Sodium Antimony Gluconate for the Treatment of Kala-Azar.** *J. Indian Med. Ass.* 1945, Sept., v. 14, No. 12, 298–9. [12 refs.]

This is a report on the treatment of 21 cases of kala azar with Stibatin (Glaxo) —a sterile solution containing 20 mgm. of pentavalent antimony per cc. The majority of the cases, which were in the Patna Medical College Hospital, were diagnosed by discovery of leishmania by sternal or spleen puncture. The full course of intramuscular injections aimed at was 2 cc. on the first day, 4 cc. on the second day, followed by 6 cc. daily for nine days (total 60 cc.). During treatment, two of the patients died (one of pneumonia and one of enteritis), and two absconded. Of the 17 patients who completed the course there was no fever in six, and in the other 11 fever disappeared in 5 to 26 days. In all cases there was increase in weight, improvement in the blood count and diminution in the size of the spleen. The series is, however, unsatisfactory, as no follow-up was made, so that in no case can it be stated that a permanent cure was obtained.

In a foot-note it is stated that larger doses are now recommended—15–20 cc. daily to a total of 150–200 cc. Daily injections of 10 cc. were tried in two cases for three days. In both, the injections were very painful, and enteritis developed. Subsequently both were cured by intravenous ureastibamine.

C. M. Wenyon.

GOODWIN, L. G. **The Chemotherapy of Experimental Leishmaniasis. II. A Dose Response Curve for the Activity of Sodium Stibogluconate.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Oct., v. 39, No. 2, 133–45, 5 figs.

In Part I of this series of papers [this *Bulletin*, 1945, v. 42, 262] the author has shown that the number of leishmania per 100 spleen cell nuclei in smears is a reliable measure of the degree of infection of Syrian hamsters infected with *Leishmania donovani*. It was also demonstrated that a single subcutaneous dose of an effective drug may have a measurable effect on the spleen count. In the present paper evidence is brought forward that these observations may be used to obtain a dose-response curve for sodium stibogluconate [sodium antimony V gluconate—" solustibosan "]. An inoculated animal becomes suitable for a test when the count shows 10 to 300 leishmania per 100 spleen cell nuclei. Following intraperitoneal inoculation, the three strains of *L. donovani* investigated reached this degree of infection in three months, six weeks and three to four weeks, respectively. The last strain is particularly useful because of the rapid development of the infection. These degrees of infection were recorded according as the parasite count gave 10, 10 to 50, 50 to 300, over 300. After various trials it was found that the action of the dose of drug administered subcutaneously could be assessed by comparing the count obtained from a spleen smear made a week after treatment with the count made from a smear of a portion of the spleen removed by biopsy on the day before treatment. From the data obtained with various doses, the dose response curves can be obtained. It was found that there was considerable variation in different tests, so that when new drugs are to be compared a number of animals from the same stock must at the same time be treated with a standard preparation, like the sodium antimony gluconate used in this investigation, the results of which show that it is possible to obtain a quantitative dose-response relationship for the leishmanicidal activity of single doses of drugs in Syrian hamsters.

C. M. Wenyon.

CANAAN, T. **Topographical Studies in Leishmaniasis in Palestine.** *J. Palestine Arab Med. Ass.* 1945, Nov., v. 1, No. 1, 4–13, 1 map. [34 refs.]

Oriental sore and kala azar are now of fairly wide distribution in Palestine. Before the 1914–18 war cases of the former disease were rarely seen outside the Jericho area. Since then there has been a steady extension from this primary focus, while Jewish immigrants from Persia, Iraq and other endemic areas have created new centres of infection. At the present time infection is present in many towns and villages in the coastal areas as well as in the mountainous districts. These are arranged in groups around some central town. Thus, the largest southern group is in the Bethlehem district, with Bêt Djâla as the centre. The next largest is the Jerusalem centre, while the Jericho centre, the original home of the disease, is a smaller one. In the north the largest centre is Haifa, where 212 cases were seen by STERNFELD [this *Bulletin*, 1944, v. 41, 551] in the period 1933–1943. The incidence of the disease in these areas is not uniform, there being a tendency for it to assume almost epidemic proportions in certain years.

Kala azar, the first cases of which were reported in 1930 and 1931, is comparatively unimportant. In all, 51 different places have supplied 67 cases, including 8 from Haifa and 4 from Bêt Iksa. It is interesting to note that in most

of the important centres of oriental sore, kala azar has not yet been identified. Kala azar in dogs has been discovered in a number of localities since the first case was seen in Jerusalem just before the recent war. During the five years of the war, 13 or more foci of canine infection have been found. It is interesting that up to the present no cases of purely cutaneous leishmaniasis in dogs have been noted, though animals suffering from kala azar may develop cutaneous lesions. It is evident that further observations are required before the complete distribution of the various types of leishmaniasis in Palestine can be estimated. The centres at present known to be infected are marked on a map of the country which illustrates the paper. *C. M. Wenyon.*

SENEKJIE, H. A. & LEWIS, Ruth A. *In vitro* **Effects of Specific Immune Blood on certain Blood and Tissue Flagellates.** *Proc. Soc. Exper. Biol. & Med.* 1945, June, v. 59, No. 2, 185–8.

The experiments described in this paper show that when immune sera are added to media in which certain flagellates are growing there is a specific action on the homologous organisms. Immune sera were prepared in rabbits by intravenous injection of cultures of three species of *Leishmania* (*L. donovani*, *L. brasiliensis*, *L. tropica*) and *Trypanosoma cruzi*. When these organisms were grown in rabbit blood agar containing 5 per cent. of immune sera it was found that the effect was very marked in the case of *T. cruzi* and *L. donovani*, but much less so in the case of *L. tropica* and *L. brasiliensis*. In each case, however, the action was on the homologous organism. The factors responsible were contained in the sera, for if washed red blood corpuscles were added to the medium instead of serum, there was no action. The factors are thermostable at a temperature of 56°C. but they are partially destroyed at 70°C. Under the action of a homologous serum the culture flagellates first lose their motility and become agglutinated, later they round up and swell, while finally, with hyalinization of the internal structures, they die. It was shown that complement is not necessary for this action, and that the active principle is different from ablastin. *C. M. Wenyon.*

DOSTROVSKY, A. **The Incubation Period in Experimental Cutaneous Leishmaniasis.** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*). 1945, Sept., v. 4, No. 9, 303–5.

The author inoculated culture forms of *Leishmania tropica* into the skin of the left upper arms of four volunteers, the doses being 16, 4, 5, and 2 million flagellates respectively. In each case there was an immediate reaction, which, in 24 hours, showed as a red area with elevated centre. Without regression, these lesions developed in the next few days into typical leishmania ulcers. It is held that the large doses of flagellates injected were responsible for the clinical absence of any incubation period. Leishmania were found in smears from three of the ulcers. The fourth was still under observation.

C. M. Wenyon.

FEVERS OF THE TYPHUS GROUP.

HAMILTON, H. L. **Specificity of the Toxic Factors associated with the Epidemic and the Murine Strains of Typhus Rickettsiae.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 391–5.

As has already been found by other workers, the complement-fixation titres of sera from patients suffering from epidemic typhus were observed to be far

higher against epidemic than murine antigens; so also the author found that the same sera neutralized much greater amounts of epidemic- than of murine-rickettsial toxins. When sera from patients suffering from endemic murine typhus were subjected to similar comparative tests it was found that the complement-fixation titres indicated a high degree of specificity, being much higher when murine antigen was used, but with the toxin-neutralizing tests the differences in titre were considerably less; in some cases the sera were capable of neutralizing only twice to four times more murine than epidemic toxin.

This incomplete degree of correlation suggested that the complement-fixing antibodies might not be the same as the toxin-neutralizing antibodies. The author concludes, however, that the toxins associated with epidemic rickettsiae are immunologically distinct from those associated with murine rickettsiae.

John W. D. Megaw.

Chung, H. L. **On the Susceptibility of *Phthirus pubis* to Infection with Typhus Virus.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 331–3.

Three batches of crab-lice were fed for seven to nine days on three typhus patients. Suspensions of the lice were inoculated into guineapigs which "showed typical febrile reactions, and, not infrequently, also scrotal swelling." Rickettsiae described as *R. prowazeki* were isolated from the guineapigs. The author suggests that in certain circumstances the crab-louse may act as a transmitter of typhus fever, but he points out that the experiments do not prove that the organisms multiply in the lice, which may have served merely as reservoirs of the infected blood. *John W. D. Megaw.*

Brug, S. L. Op Rickettsia gelijkende vormsels in de menschelijke long. [**Rickettsia-like Bodies in the Human Lung.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1941, Dec. 20, v. 85, No. 51, 4636–9, 9 figs. (8 coloured) on 1 pl. English summary.

"Description of intracellular granules found in sections as well as in smears of human lungs. The granules greatly resemble Rickettsia. In 21 lungs collected at random they could be found in every case either in the smears or in the sections or in both. Probably they are normal elements of the lungs. When one is searching for virus in human material they may be mistaken for Rickettsia."

Ionesco-Mihaiesti, C. & Ciuca, M. Contribution à l'étude histopathologique de la pneumonie expérimentale chez la souris par instillation nasale de Rickettsia Prowazecki. [**A Contribution to the Study of the Histopathology of Experimental Pneumonia of Mice Infected by the Nasal Route with *Rickettsia prowazeki*.**] Reprinted from *Arch. Roumaines Path. Expér. et Microbiol.* Bucharest. 1943, Jan.–Dec., v. 13, Nos. 1/2, 1–43, 52 text figs. & 17 coloured figs. on 9 pls. [15 refs.]

This monograph is profusely illustrated by 52 photomicrographs and 17 excellent coloured drawings. Full details are given of the technique employed including the use of a panchromatic stain whose composition is methylene blue 1·0 gm., toluidine blue, 0·25 gm., thionine, 0·25 gm., azure I, 1·0 gm., McNeal's methylene violet, 0·5 gm., and scarlet eosin, 0·75 gm. dissolved in a mixture consisting of methyl alcohol, 300 cc., glycerin, 200 cc., and acetone, 60 cc. Fifteen drops of the stain are added to 10 cc. distilled water. Sections are stained for one or two hours, washed in distilled water, dehydrated in absolute alcohol for one or two seconds, then treated with a mixture of one part

oil of cloves in nine parts absolute alcohol till the sections assume a violet tint. After passing through three baths of xylol the sections are mounted in Canada balsam.

The immediate effects produced on mice by the intranasal instillation of three or four drops of suspension of heavily infected mouse lung are severe, sometimes fatal, shock. When the animal recovers from this there is very soon an intense mobilization of polymorphonuclear leucocytes in the capillaries and walls of the alveoli; the rickettsiae are subjected to active phagocytosis by these leucocytes in whose cytoplasm they multiply rapidly, causing disintegration of the cells. Within 10 hours or so large mononuclear wandering cells begin to replace the polymorphonuclears, and in turn become destroyed by the multiplication of the rickettsiae. After about 40–48 hours the fixed endothelial cells of the arteries become invaded by rickettsiae, which multiply enormously in the cytoplasm, often pushing the nuclei to one side, and finally either rupturing the cell wall or replacing the cell by a dense mass of the organisms. These cells correspond to those described by MOOSER as occurring in the peritoneum of rats, and the tunica vaginalis of guineapigs, inoculated by the intraperitoneal route with living rickettsiae.

The cell contents, on being discharged into the alveoli and bronchioles, fill these with a sero-sanguineous fluid rich in rickettsiae.

The epithelial cells of the air passages were never invaded by rickettsiae even when large numbers of these were brought into close contact with the cells. *John W. D. Megaw.*

BABLET, J. & GIROUD, P. Étude histologique des lésions pulmonaires provoquées chez le lapin par l'inoculation intratrachéale expérimentale de virus du typhus épidémique. [**Histological Study of Pulmonary Lesions in Rabbits due to Intratracheal Inoculation of Epidemic Typhus Rickettsiae.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 11/12, 344–7, 4 figs. on 2 pls.

AUBIN, H. Notes sur les psychoses du typhus exanthématique. [**Notes on the Psychoses of Exanthematic Typhus.**] *Méd. Trop.* Marseilles. 1945, Jan.–Feb.–Mar., v. 5, No. 1, 54–64.

The author gives numerous examples of the various psychoses encountered in typhus fever during the incubation stage, the period of defervescence, and early and late convalescence. Cases are described as occurring during inapparent attacks in which the real nature of the illness would have been overlooked if suspicion had not been aroused; in such cases a diagnosis may be impossible unless laboratory tests are carried out.

The psychoses are not, as is often stated, necessarily of the confusional type. There is sometimes evidence to show an inherited predisposition to psychosis, but often the attack of typhus fever appears to be the sole cause, and when this is so the prognosis is naturally more hopeful. *John W. D. Megaw.*

GIROUD, P. & GIROUD, M.-L. Agglutination des rickettsies, test de séro-protection et réaction d'hypersensibilité cutanée. [**Rickettsia-Agglutination Test; Serum-Protection Test; and Reaction of Cutaneous Hypersensitivity.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 3/4, 84–93, 1 fig.

Large numbers of the tests were carried out, many of them comparative.

The rickettsia-agglutination test employed was a modification of the original Weigl test. Rickettsia suspensions were made from infected mouse lungs which were ground up in formolized saline, and freed from large particles by decantation. Seven droplets of the suspension were placed separately on a slide, and to each was added a droplet of one of seven dilutions of the serum

to be tested, ranging from 1–10 to 1–640. The slide was at once placed in a Petri dish containing a little water to prevent evaporation. After 12 hours at room temperature the slide was taken out and the droplets were allowed to dry. The films were fixed in methyl alcohol, washed in water, and stained for half an hour with a mixture of five drops of Giemsa stain and 1·0 cc. " boiling " neutral distilled water. After differentiation in equal parts of absolute alcohol and xylol, the film was washed and dried. The degree of agglutination is said to be sharply defined, ranging from coarse dense clumps to very small clumps among scattered free organisms.

The tests of human sera were carried out immediately before each of three injections of rabbit-lung vaccine, given at weekly intervals, and a week after the last injection. The highest titre was usually reached a week after the second dose of vaccine, but the responses were very varied, the titres ranging from 1–10 to 1–640 and averaging 1–80 to 1–160. The sera of patients suffering from severe attacks of typhus fever reacted at high titres, such as 1–1,500 ; in mild, " pseudo-influenzal", attacks the titres usually were 1–80 to 1–160. The reaction soon became negative.

The serum-protection tests were carried out by mixing the serum with varying dilutions of virulent rickettsial cultures, keeping the mixtures for half an hour at 37°C., and injecting them intradermally into a rabbit. As a control the same culture, without serum, was injected into another part of the skin of the same rabbit.

The sera of vaccinated persons showed protective reactions of progressively increasing strength after successive doses of the vaccine. After mild attacks of typhus, corresponding reactions occurred ; after severe attacks still stronger reactions were observed, and they remained positive for many years.

The intradermal hypersensitivity test is based on the local inflammatory reaction produced in typhus patients by intradermal injections of killed rickettsia cultures. This reaction gave very varying results ; it usually remained negative after protective vaccination with killed rickettsiae, but after vaccination with living rickettsiae, and after mild attacks of typhus, it soon became positive. After severe attacks the reaction was slow in appearing, sometimes it was delayed for months. It remained positive for years after the attack.

There was no agreement between the responses to the serum-protection and rickettsia-agglutination tests ; the latter gave irregular and inconsistent results, but the serum-protection test gave results consistent with the amount of antigen injected. The rickettsia-agglutination test was regarded as indicating the presence of " antibodies of infection " rather than of immune antibodies. *John W. D. Megaw.*

SUREAU, B. Élimination d'agglutinines antirickettsies par les urines albumineuses du lapin inoculé par voies dermique ou péritonéale. [**Discharge of Anti-Rickettsial Agglutinins through the Albuminous Urine in Rabbits Inoculated Subcutaneously and Intraperitoneally.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 7/8, 185–7, 1 fig.

Rabbits were inoculated with living typhus rickettsiae ; when the agglutination titre of the serum had reached a height of about 1–160 an artificial nephritis was produced by a bismuth preparation injected daily for a week. When the albuminuria became pronounced, agglutinins appeared in the rabbits' urine, reaching a titre of rather less than 1–40, and simultaneously the agglutination titre of the serum fell to less than 1–80. With the disappearance of the albuminuria the agglutinins also disappeared from the urine and the agglutination titre of the serum rose slightly, remaining constant for some time at about 1–80. *John W. D. Megaw.*

GIROUD, P. & SUREAU, B. Les variations des agglutinines de la peau inoculée et saine chez le lapin infecté par voie dermique avec du virus typhique. [**Variations in Agglutinins from Inoculated and Healthy Skin in Rabbits Injected Intradermally with Typhus Rickettsiae.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 9/10, 264–6, 1 fig.

v. BORMANN & PREUSS. Zur Schnelldiagnose des Fleckfiebers aus dem Blutstropfen. [**The Rapid Diagnosis of Typhus Fever by Blood Droplets Slide Test.**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1944, Nov. 16, v. 105, No. 4, 313–30, 1 fig. [11 refs.]

The most useful feature of this paper is that it contains a summary of the numerous rapid modifications of the Weil-Felix and other agglutination tests. The authors give details of the method adopted by themselves in carrying out one of these modified tests, in which dried cultures of *Proteus OX19*, prepared by a proprietary firm, are used for the suspensions. They lay special stress on the employment of drops of suspension not larger than the drops of blood under test.

Their claim that the test is more reliable than the standard test does not appear to be valid. Among 46 patients, suffering from diseases other than typhus fever and tested by their method, there were 19 positive reactions as compared with four with the standard test. Although they claim that in 378 samples of blood from typhus patients there were 103 negative responses as compared with 121 with the standard test, the basis of comparison seems to be unfair because no account is taken of standard reactions at titres below 1–400 ; all these are included among the negative responses and their number is not stated. *John W. D. Megaw.*

ORTIZ-MARIOTTE, C., MALO-JUVERA, F. & PAYNE, G. C. **Control of Typhus Fever in Mexican Villages and Rural Populations through the Use of DDT.** *Amer. J. Pub. Health.* 1945, Nov., v. 35, No. 11, 1191–5, 1 fig.

In two Mexican villages, epidemics of typhus fever were promptly controlled by dusting the clothing of the great majority of the inhabitants with a powder containing 5 per cent. DDT. In one village 612 of the 671 inhabitants were treated, and in another 739 out of 1,016. Each person's head was treated with a lotion whose active principle was phenyl cellosolve [see this *Bulletin*, 1944, v. 41, 744]. In both villages the disinfestation was started while the epidemic was approaching its peak, and, allowing for the incubation period, the abrupt cessation was what would have been expected, assuming complete efficiency of the method.

Experiments were carried out in typhus-free villages ; in one with a louse-infestation rate of 33 per cent. the clothing was treated twice, with a seven-day interval ; two weeks later the infestation rate was 1·6 per cent. ; six weeks later it was 1·1 per cent. ; three months later it had risen to 9·5 per cent. In another village a single treatment reduced the rate from 60 to 11 per cent. ; two months later it had risen to 26 per cent.

The effect of phenyl cellosolve on head lice was only temporary.

John W. D. Megaw.

NEUJEAN, G. Études sur les Rickettsioses. I. Note préliminaire. II. Problèmes posés. Critique des méthodes. Nouveaux procédés de diagnostic et de recherche. [**Studies of the Rickettsial Diseases. I. Preliminary Note. II. Problems Presented ; Critical Review of Methods ; New Methods for use in Diagnosis and Research.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 5–9 ; 10–22.

Some of the findings and expressions of opinion presented in these papers are so revolutionary that they are not likely to be generally accepted without confirmation.

In Part I the author refers to his previous description of an epidemic in Ruanda-Urundi in 1939–40; in this the rickettsiae were regarded as being murine though they seldom caused an orchitic reaction and were abnormal in some other respects. The organisms were isolated from lice, bed-bugs, fleas, and ticks; in some of the outbreaks the vector chiefly incriminated was the bed-bug. The mammalian reservoir was the rat in which a very high percentage rate of infection was found in the affected areas. The Weil-Felix reaction was of the *Proteus OX19* type, but in recent outbreaks the *OXK* type has become increasingly frequent. Few fatalities occurred, but in some severe attacks an "inoculation eschar," like that of boutonneuse fever, was seen.

In Part II the opinion is expressed that rickettsiae are closely related to protozoa. The fallacies connected with the usual methods of diagnosis and research are discussed, including the anomalous results often obtained by animal experiments and the Weil-Felix test. Strict adherence to the technique of Felix and Bridges [this *Bulletin*, 1944, v. 41, 552 & 554] is recommended.

Great advantages are claimed for the staining method of Lestoquard; briefly, this consists in fixing for 5–10 minutes in a mixture of 98 parts of 94 per cent. alcohol and two parts of "fresh tincture of iodine"; washing in alcohol; drying; staining for one or two hours in a mixture of 1·0 cc. distilled water (*p*H 7·4) and three drops each of May-Grünwald and Giemsa stain; differentiation by alcohol; and washing in neutral distilled water. Using this method, the author claims to have shown the frequent presence of rickettsiae, in the urinary sediment obtained by centrifugation, in the sputum, the conjunctival secretion, the nasal mucus, and in skin scrapings obtained by the method used in the search for leprosy bacilli.

He states that rickettsiae can easily be cultivated by adding the patient's blood to normal saline; great multiplication of the organisms is said to occur in the infected white cells within a period ranging from a few hours to two or three days.

The most surprising claim of all is that during the prevalence of the disease of Léopoldville, rickettsiae were found in the blood of all the 50 persons examined, whether they were sick or healthy. This universal occurrence of the organisms is regarded as being comparable with what happens in malaria [presumably in areas of hyperendemicity].

Examination of the urine gave positive results only when the disease process was active. Pronounced rickettsial infection was found in the liver cells of patients who had been retrospectively diagnosed as suffering from yellow fever because of the histological changes found in the organ. *John W. D. Megaw.*

Pang, K. H. **Studies on Typhus Fever Epidemic occurring in a Poor House. II. Etiological and Epidemiological Studies.** *Chinese Med. J.* Washington. 1944, Oct.-Dec., v. 62, No. 4, 334–46. [23 refs.]

This epidemic occurred in a poor-house where 570 persons were living in deplorable conditions in rooms infested with rats. The conditions appear to have been eminently suitable for the occurrence of both louse-borne and flea-borne typhus.

Among 248 children under 11 years, there were 11 cases; in the 11–15 age group there were 23 cases among 196 children, and among the remaining 130 persons there were 4 cases.

Two girls living in one room were attacked on April 5, 1940; another girl in the same room was attacked on May 26, and then cases began to occur in various rooms. After August 22 there were no further cases till April 25, 1941, when three girls occupying a rebuilt and relatively rat-free room were attacked; and during the next two months six further cases occurred.

Numerous strains of rickettsiae were isolated by guineapig inoculation; of these, seven were from patients, eight from rats and their fleas, four from body lice of patients, ten from body lice of healthy inmates, and one from a rat mite.

Obvious orchitis appears to have occurred in only one of the many guineapigs used for inoculation or transfer of the strains, but rickettsiae were often detected in vaginal smears. The infection is stated to have died out after a few passages in guineapigs.

During the period of the main epidemic only four of the 18 rats examined were infected, and in the inter-epidemic period seven of 12 rats were found infected.

Inoculation experiments with batches of lice collected from healthy inmates gave the following results—one batch collected May 18, 1940, was infected; two batches collected June 17 and 25, 1940, at the height of the epidemic, were infected; only one among ten batches collected during the winter-epidemic period up to January 1941 was infected; between February and April 1941 "most of the batches examined were infected," and during the recrudescence of the infection all the three batches tested were infected.

All the strains isolated were regarded as murine, but transmission was believed to be by lice. *John W. D. Megaw.*

Pang, K. H., Zia, S. H., Chen, S. M. & Feng, Y. S. **Studies on Typhus Fever Epidemic occurring in a Poor House. III. Control Measures, with special reference to the Use of Typhus Vaccine.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 347–50.

The author describes the results obtained by the use of a locally prepared tissue-culture vaccine in the control of an institutional epidemic.

Among 97 vaccinated girls there were five attacks (5·2 per cent.) against nine attacks (9·5 per cent.) among 105 non-vaccinated girls living in closely similar conditions. No mention is made of any difference in the severity of the attacks in the two groups; the disease is stated to have been mild, and there were no deaths. [Part I of this series has not been traced, the reference to it as given by the authors is incorrect.—*Ed.*] *John W. D. Megaw.*

Rugiero, H. R. & Cohen, J. Nuevos casos de tifus exantemático en la Ciudad de Buenos Aires y sus alrededores. [**Further Cases of Exanthematic Typhus in Buenos Aires and its Environs.**] *Prensa Méd. Argentina.* 1945, Nov. 9, v. 32, No. 45, 2203–5.

The authors have seen 11 cases of murine typhus fever in and near Buenos Aires between August 1944, and July 1945.

The cases were sporadic, but six of the patients, who were attacked in January and February 1945, had been working on the same floor of a rat-infested grain store. *John W. D. Megaw.*

Anderson, W. L. & Wing, W. M. **Tsutsugamushi Disease (Scrub Typhus): a Clinical Study of Forty-Nine Cases.** *War Medicine.* Chicago. 1945, Sept., v. 8, No. 3, 163–6.

Brief clinical notes are given of 49 cases of tsutsugamushi fever, which occurred in a Pacific Island among 750 soldiers who had bivouacked on a grassy plain previously occupied by Japanese troops.

The percentage incidence of the chief features was—headache, 98; backache, 90; chills, 30; deafness, 15; respiratory-system involvement, 10; adenopathy

90; eschar, 70; rash, 43; palpable spleen, 40; tender lymph nodes, 35, bradycardia, 100; *Proteus OXK*-agglutination reaction, 53; leucopenia, 40; minor abnormality of urine, 30.

In many cases there were multiple eschars. A reference is made to the occurrence of "infected bites of men from the same patrol, hospitalized for other causes." These lesions are said to have had a different distribution on the body, but they are not described.

The island had been reported to be free from infection and the authors remark that "if that is true it must be assumed that the disease had been introduced by the Japs," but he rightly suggests as a much more likely explanation that the disease had existed without being recognized.

John W. D. Megaw.

Howell, W. L. **Absence of Electrocardiographic Changes in Tsutsugamushi Fever (Scrub Typhus). Report of Two Hundred Consecutive Cases.** *Arch. Intern. Med.* 1945, Oct., v. 76, No. 4, 217–18.

"1. An electrocardiographic study was made of 200 consecutive patients convalescent from tsutsugamushi (scrub typhus) fever.

"2. No abnormal electrocardiographic patterns were found.

"3. The incidence of isolated deviations from the normal was no higher than that found in the electrocardiograms of healthy persons of the same age."

Blake, F. G., Maxcy, K. F., Sadusk, J. F., Jr., Kohls, G. M. & Bell, E. J. **Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea.** *Amer. J. Pub. Health.* 1945, Nov., v. 35, No. 11, 1121–30, 1 map. [25 refs.]

This is a review article; most of the information has already been abstracted, see this *Bulletin*, 1945, v. 42, 991, 993.

Somers, R. B. U. **A Case of Tick Typhus in the Sudan.** [Memoranda.] *Brit. Med. J.* 1945, Dec. 15, 848, 1 chart.

The special interest attaching to this case is that it is the first to be reported from the Anglo-Egyptian Sudan. The patient was an English schoolmaster, engaged in inspecting bush schools.

The fever was predominantly of a deep remittent type. It lasted about 10 days. The pulse rate was slow, never exceeding 76; on one occasion, when the temperature was 103°F., it was 64.

A *tache noire* was present; this had been seen by the patient about 10 days before the onset; no tick had been detected. There was a maculo-papular rash, with a tendency to vesication in some of the spots; the rash was abundant on the forearms and scanty on the trunk. *Proteus OX2* was agglutinated at a titre of 1–500; with *OX19* the reaction was negative.

John W. D. Megaw.

Le Gac, P. & Borjeix, L. Premier cas de fièvre boutonneuse au Togo. [**The First Case of Boutonneuse Fever in Togo.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 247–50.

Bow, M. R. & Brown, J. H. **Tick-borne Diseases of Man in Alberta.** *Canadian Med. Ass. J.* 1945, Nov., v. 53, No. 5, 459–65, 1 map. [48 refs.]

The authors give short notes on the history, epidemiology and clinical aspects of Rocky Mountain spotted fever, tick paralysis, and tularaemia, with

special reference to their occurrence, since 1938, in the Province of Alberta, Canada. Six known cases and one suspected case of Rocky Mountain spotted fever have been reported in Alberta, there have been two cases of tick paralysis, and two cases of tick-transmitted tularaemia in man. In the authors' opinion the tick-borne diseases of man are important in Alberta ; they appear at present to be confined to the southern part of the Province " but there are indications that further survey work might disclose a similar situation in the foothills and mountain area."

The following ticks capable of transmitting tularaemia have been collected in Alberta :—*Dermacentor andersoni*, *Haemaphysalis leporispalustris* (rabbit tick), and *Haemaphysalis cinnabarina* (bird tick). *D. andersoni* infected with *Dermacentroxenus rickettsi* [*Rickettsia rickettsi*] and with *Pasteurella tularensis* has been collected in the southern area of the Province.

[Parker *et al.* (*Public Health Reports*, Washington, 1932, v. 47, 479) found strong presumptive evidence that *H. cinnabarina* transmitted tularaemia in sage hens, but no proof that it had been implicated in human disease.]

J. F. Corson.

Parrot, G. La " fièvre des tranchées " existe-t-elle en Algérie ? [**Does Trench Fever occur in Algeria ?**] *Arch. Inst. Pasteur d'Algérie.* 1945, Sept., v. 23, No. 3, 180–82, 1 chart.

The author describes a case of fever which conformed in all its clinical features to one of the types of trench fever. There were three spells of fever, each lasting about three days ; the spells started on the 1st, 7th and 14th days. The fever curve was of the undulant type, and the total duration was 14 days.

Severe nocturnal pains of the shin-bone type occurred, and convalescence was slow. Repeated blood examinations, including culture tests, gave negative results, and the author was satisfied that relapsing fever, undulant fever, malaria, and typhoid-group fevers could be excluded. He suggests that some of the numerous cases diagnosed in Algeria as " relapsing fever without spirochaetes " may be examples of trench fever. *John W. D. Megaw.*

YELLOW FEVER.

Bates, M. & Roca-Garcia, M. **The Douroucouli (Aotus) in Laboratory Cycles of Yellow Fever.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 385–9, 2 figs.

" Four douroucoulis (*Aotus trivirgatus*) from the Villavicencio area of eastern Colombia were tested in laboratory cycles of yellow fever with the mosquito *Haemagogus capricornii* and a local strain of virus. All four animals showed acute, fatal infections, characterized by fever and a very high titer of circulating virus ; death occurred on the fourth or fifth day after infection. Three of the animals showed stomach hemorrhage, and liver tissue from all four showed lesions characteristic of fatal yellow fever in man and rhesus monkeys. Virus was transmitted by the bite of the mosquito *Haemagogus capricornii* from saimiri to douroucouli, douroucouli to douroucouli, and douroucouli to saimiri. There is some evidence that the douroucouli may be important in the epidemiology of yellow fever, since it is said to be the only monkey in certain areas in Columbia where the disease is endemic."

FERRERO, A. L'*Aedes aegypti*. Le danger qu'il représente pour l'agglomération Algéroise. [*Aëdes aegypti:* **its Danger to Algeria.**] [Thesis.] 100 pp., 1 folding map & 4 figs. [Bibliography.] 1939. Algiers: La "Typo-Litho" et Jules Carbonel réunies.

FAVAREL, R. Immunisation du cobaye contre le virus de la fièvre jaune par scarifications cutanées. [**The Immunization of the Guineapig against Yellow Fever Virus by Cutaneous Scarification.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 3/4, 77–86.

The author inoculated 11 guineapigs with neurotropic yellow fever virus, the French strain at its 218th passage in mice; and 6 guineapigs with culture virus 17D, reinforced by 10 mouse brain passages and growth again on chick embryo. In both series the cutaneous scarification method was used.

Out of the 11 animals vaccinated in this manner with the neurotropic virus, 7 were completely resistant to an intracerebral inoculation of several thousand lethal doses 35 to 47 days after being immunized. On the contrary, all 6 guineapigs vaccinated in the same way with the culture virus succumbed to yellow fever encephalitis when inoculated intracerebrally with virus 25 to 50 days after the scarification. Out of 5 guineapigs scarified with neurotropic virus, which all gave negative mouse protection tests, two were resistant when inoculated intracerebrally with the virus, showing that an animal may be immune without the blood containing immune bodies in sufficient quantity to give a positive test.

The divergent results obtained with these two strains may be explained as due to the difference in neurotropism. One could also suppose that one strain had a greater affinity for the skin of the guineapig.

In the discussion Dr. STEFANOPOULO, in whose laboratory the work was performed, emphasized that in the case of bacterial infections it is necessary to use a larger dose of an attenuated strain than of a virulent strain in order to produce infection. Normally, the guineapig is not very susceptible to yellow fever virus, and with culture virus it is probably necessary to use larger doses to produce immunity. He also mentioned that vaccination of human beings with culture virus by the scarification method is often insufficient to ensure protection, but that subcutaneous inoculation of the same virus is efficacious. *E. Hindle.*

DENGUE AND SANDFLY FEVER.

FAIRCHILD, L. M. **Dengue-like Fever on the Isthmus of Panama.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 397–401, 3 figs.

The author studied 32 cases of a short fever seen in the Panama-Canal Zone between September 1941, and March 1942.

Among 21 cases in which the fever curve was available 13 were of the two-phase, "saddle-back", type and 7 of a "continuous spiking" type. The total duration of the fever in both types was about five days.

A blotchy macular rash was seen in every case. One or more groups of lymph nodes were enlarged in five cases. The leucocyte count ranged from 2,000 to 8,000 per cmm.; the lymphocytes were more than 40 per cent. of the total white cells in the 16 cases in which there was leucopenia.

The author discusses at some length the features in which the symptomatology differed from that described by certain authors as being characteristic of

dengue, but in view of the well-known variability of that disease, and of the known occurrence of outbreaks in the region, there seems to be no good reason for hesitating to place the fever in the dengue group. *John W. D. Megaw.*

CULLINAN, E. R. **Immunity to Sandfly Fever [Memoranda.]** *Brit. Med. J.* 1946, Jan. 5, 12.

An outbreak of sandfly fever occurred in a hospital in the Middle East in the summer of 1942 [see CULLINAN & WHITTAKER, this *Bulletin*, 1944, v. 41, 126] and in the summer of 1943 another outbreak occurred in the same hospital. In the first outbreak several persons had more than one attack, which suggested that an attack conferred no early immunity.

In the second outbreak, in 1943, 55 out of 142 [about 39 per cent.] of persons who were not present during the 1942 outbreak were attacked while only 13 out of 98 persons [about 13 per cent.] who were present in 1942 were attacked. The author thinks that this evidence suggests that while an attack of sandfly fever does not confer an early immunity, or at most a very short-lived one, it may confer a more distant immunity. [See also LIVSHITZ, this *Bulletin*, 1944, v. 41, 566.] *J. F. Corson.*

PLAGUE.

DEVIGNAT, R., SCHOETTER, M. & GILLE-SIMUL, Mme. S. Quelques considérations sur la peste du cobaye. [**Notes on Plague in the Guineapig.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 25–36, 3 diagrams.

A periodic extraction of data from routine records is a useful and serviceable exercise, especially when assisted by personal memory. In the campaign against plague on Lake Albert in the Belgian Congo the laboratory at Blukwa has played a notable part. Since 1936 more than 12,000 guineapigs have been inoculated in various ways with plague material, and more than 600 of these, dead of plague, have been subjected to autopsy. The different modes of inoculation are classified as : subcutaneous, conjunctival, on scarified skin, and other ways. The discussion in the text, accompanied by graphs and detailed tables, relates to :—A. Standard infecting dose ; B. Inoculation by different methods ; and C. Data of preventive vaccination and serum prevention. This discussion is summarized :—(1) Autopsies showed three different types : (*a*) the violent septicaemia with hypertrophy of liver and spleen ; (*b*) the moderate form in which liver and spleen are enlarged and mottled ; and (*c*) that of partial resistance, where liver and spleen seem pseudotuberculous, while the lung is consolidated (hepatization) and covered with whitish tubercles. (2) The duration of life is shown as a graph of the number of guineapigs dead on each successive day after a virulent inoculation. "With a strain of maximal virulence," say the authors, and "inoculation of 10 lethal doses (54 to 155 organisms) we obtain a curve which we put forward as a unit of virulence," for the determination of the severity of routine inoculations and ultimately of protection by vaccine or serum. The authors consider that this graphic method is more expressive than the simple presentation of the crude figure giving the percentage of animals dead and surviving. *W. F. Harvey.*

COLE, L. C. **The Effect of Temperature on the Sex Ratio of *Xenopsylla cheopis* recovered from Live Rats.** *Pub. Health Rep.* Wash. 1945, Nov. 9, v. 60, No. 45, 1337–42. [14 refs.]

The danger of plague in an area is often considered to be proportional to the flea population, particularly of *Xenopsylla cheopis*. The flea population is usually estimated by " flea counts " from trapped rats, but these counts do not always give an accurate estimate of the total natural population. This paper attempts to relate the results of flea counts to the total flea population, and to show how temperature changes in the environment may affect the results. Male and female fleas apparently exist in approximately equal numbers, but whereas at low temperatures (below 70°F.) females usually predominate in captures from rats, at high temperatures (over 75°F.) males are caught in greater numbers. This rise in the proportion of males captured at higher temperatures is due to an increase in the number of males found on the rats, rather than to a fall in the number of females. It is suggested that the " flea index " should perhaps be computed for female fleas only. *Kenneth Mellanby.*

KALMBACH, E. R. **" Ten-Eighty", a War-Produced Rodenticide.** *Science.* 1945, Aug. 31, 232–3.

The substance referred to is sodium fluoroacetate. Its toxicity to small mammals was found during the course of the long-established search for new rodenticides carried out by the Wildlife Research Laboratory in Denver. Compound " 1080", as it is known, is extremely toxic to many small mammals and also to domestic animals such as cats and dogs, and is a possible danger to man, especially to operators who may use it carelessly. The following table gives the LD50 values :—

	Mg/kg.
" Leghorn hens	10·00
Deer mice (*Peromyscus*)	5·0
Wood rat (*Neotoma*)	5·0
Wild Norway rats (*R. norvegicus*) ...	5·0
Tame white rats	2·5
Black-tailed prairie dogs (*C. ludovicianus*)	2·5
Meadow mice (*Microtus*)	0·5
Domestic dogs	0·35
Fisher's ground squirrel (*C. beecheyi fisheri*)	0·35
Wild black rats (*R. rattus* subsp.) ...	0·1 "

Compound 1080 is very soluble in water, and the results, in rat control, of exposing a solution have seldom, if ever, been matched by other control methods. Similar results have been recorded when the material has been used on grain baits against field rodents. *Charles Wilcocks.*

RICHTER, C. P. **The Development and Use of Alpha-Naphthyl Thiourea (Antu) as a Rat Poison.** *J. Amer. Med. Ass.* 1945, Dec. 1, v. 129, No. 14, 927–31. [Refs. in footnotes.]

This paper contains the first detailed announcement of the development of a new rodent poison by a team of the Johns Hopkins University, working under a contract with the Office of Scientific Research and Development. Alpha-naphthyl thiourea is a fine grey powder, highly insoluble in water or acid solutions ; slightly more soluble in alkalis ; stable under normal conditions, and with a melting point of 184°C. It is said to have the following LD50, though the details of toxicity tests on which such figures are based are not given :

Rattus norvegicus 7 mgm. per kilo; *Rattus rattus*, squirrels and guineapigs 100–400 mgm. per kilo; mice and dogs less than 100 mgm. per kilo. Monkeys, rabbits and chickens were more resistant and "5 Gm. per kilogram was required to kill 100 per cent. of groups of chickens and monkeys." In an extensive campaign in Baltimore it has been used in a mixture (2 to 5 per cent.) with finely ground grain such as maize or wheat and as a dust either on vegetable foods or blown in runways or on the surface of water. These tests have been in most areas 90 per cent. effective, though no detail is given as to how such estimates were arrived at. In Norway rats and dogs, death is due to drowning from pulmonary oedema, a very large lymph flow through the capillaries of the lungs being produced. No antidote is known, though the low solubility of the compound makes stomach lavage a useful countermeasure in cases of accidental poisoning. *R. B. Freeman.*

CHOLERA.

Felsenfeld, O. & Young, Viola M. **Simultaneous Vaccination against Bacillary Dysentery and Cholera with Toxoid-Vaccine.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 421.

Experiments were made to produce a reliable combined vaccine against cholera and bacillary dysentery; *Vibrio cholerae* (Inaba, Ogawa and El Tor strains), *Shigella dysenteriae* and *Sh. paradysenteriae* Y were used.

Sh. dysenteriae.—Several methods of preparation were tried and it was found by mouse protection tests that the strongest immunity was produced by a combination of alcohol-killed organisms and formolized culture filtrate.

Sh. paradysenteriae Y.—The same procedures were used except that culture filtrate was not tried; the most effective vaccine was prepared from alcohol-treated organisms.

V. cholerae.—The best results were obtained with formol-killed or heat-killed Inaba organisms combined with formolized filtrate of Inaba or El Tor strains (the El Tor strain being finally selected).

All vaccines retained their immunizing power much longer when desiccated in a vacuum.

Tests on volunteers showed that formolized organisms combined with formolized filtrate gave rise to the strongest and most lasting antibody production. A mixture of antidysentery and anticholera vaccines did not cause more severe reactions than either alone and produced a satisfactory increase of antibody formation which persisted for a considerable length of time.

The findings indicate that continuation of these experiments is fully warranted. *J. F. Corson.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Tsuchiya, H. **Survival Time of Trophozoites of *Endamoeba histolytica* and its Practical Significance in Diagnosis.** *Amer. J. Trop. Med.* 1945, May, v. 25, No. 3, 277–9.

The author has studied *E. histolytica* as it occurs in stools kept at room temperature (22°–25°C.), incubator temperature (37°C.) and refrigerator temperature (5°C.). At room temperature the survival time of six different strains

was 6 to 16 hours. In the refrigerator it was 48 to 96 hours, while in the incubator it was only 3 to 5 hours. It is evident that for diagnosis the best procedure is to examine the fresh specimen, but if this must be kept before examination, it may be left at room temperature for a few hours ; if a longer delay is contemplated then the refrigerator is the best. In no case should the specimen be left in the incubator. Amoebae which were quite motionless after exposure to cold often resumed their activities when examined in the warm chamber. In some cases amoebae which were unidentifiable in the kept stool regained their specific characters when cultivated in suitable media. A strain of trichomonas was found to survive for 21 days at 5°C. and for 15 days at 22°C. When the stool was exposed to 37°C. the organism multiplied profusely for a few hours and then disappeared. *C. M. Wenyon.*

Tan, C. C. & Liu, Y. **Amebic Colitis with special reference to Perforation. A Study of 20 Autopsied Cases.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 366–76, 6 figs.

Autopsy was done on twenty cases of amoebic colitis, in all of which there had been clinical evidence of the condition during life. The ages of the 349 patients from whom these were obtained ranged from 3 to 62 years, the majority being in their fourth decade. In half the cases coming to autopsy there was diffuse amoebic involvement of the colonic tract ; involvement of the sigmoid was seen in 17 of the 20 (85 per cent.) ; of the caecum in 16 (80 per cent.) ; of the rectum, ascending and descending colon each in 15 (75 per cent.) ; and of the transverse colon in 12 cases (60 per cent.). The terminal ileum was involved in 7 (35 per cent.), and liver abscesses were found in 6 of the 20 cases, all being in the right lobe of the liver. In 11 of the 20 cases the fatal attack of amoebic dysentery was the first attack, and in 6 of these clinically primary cases there was perforation of the gut. In 3 other cases of perforation there was a history of amoebic dysentery before the fatal attack.

A diagnosis of perforation was made *ante mortem* in 6 of the 9 cases where its occurrence was established *post mortem* ; and 8 of the 9 had received emetine either just before or after the perforation occurred. The ninth patient was moribund on admission and died in a few hours. Only one of the authors' diagnosed cases of amoebiasis with intestinal perforation recovered, and here spontaneous discharge of a localized abscess took place through the abdominal wall. In 5 of the total 10 (including the patient who recovered) the perforation occurred in the caecum ; in 4 in the descending colon ; in 2 in the sigmoid ; and in one in the transverse colon. Multiple perforation was found in 2 cases. The authors regard this complication as almost invariably fatal ; its diagnosis is difficult, and its treatment with emetine ineffective. *A. R. D. Adams.*

Cottrell, J. D. & Peddie, J. J. G. **The Diagnosis and Treatment of Chronic Amoebiasis.** *New Zealand Med. J.* 1945, Oct., v. 44, No. 243, 230–41.

This paper has been written to acquaint the medical practitioner with the problems of amoebiasis in the returned soldier. It gives a good account of the condition, but contains nothing original other than such statements as " no soldier with recurrent or chronic diarrhoea should ever be dismissed as incurable until he has had the benefit of at least one full course of anti-amoebic treatment " —in spite of repeated negative stool examinations ; and, speaking of emetine, " In emergency one or two doses may be given intravenously " ; and again, of quinoxyl enemata, " Even a 10% solution may be used in refractory cases."

A. R. D. Adams.

HOWELLS, G. **Two Cases of Amoebic Granuloma.** *Brit. Med. J.* 1946, Feb. 2, 161–2.

BRUECKMANN, G. & WERTHEIMER, E. **A Study in the Toxicology of Emetine.** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*). 1945, Sept., v. 4, No. 9, 291–4.

It has been repeatedly said that the therapeutic effect of emetine would probably be much greater if the tolerated and toxic doses were more widely separated. It was for long known to be a " general irritant and protoplasmic poison " and more recently damage to the heart and the cornea has been described. The authors have taken in hand a more intensive study of the drug toxicologically, as regards its impairment of liver function and its influence on carbohydrate metabolism, the part played by the liver in detoxification of emetine and the influence of diet on the toxicity of the drug.

Male white rats were the animals used. [The description of the results is confusedly written. Thus, the authors state : " a single high dose of emetine was given and the animals were killed from 2 to 17 hours later," and they continue directly as follows], " The higher dose, 2·0 mgm. per 100 gm. rat was always fatal in 5 days," smaller doses, 0·6–1·3 mgm. resulted in symptoms of emetine poisoning, but were not fatal. The higher doses caused a marked fall in liver glycogen, smaller doses less. Because the body temperature fell sharply this was considered to be due, not to any specific action of the drug, but to shock. To distinguish the specific influence of the drug in small doses on carbohydrate metabolism, animals were injected with doses of 0·3 mgm. and one such and one of a control group were sacrificed for glycogen determination. Under these conditions the temperature remained unchanged for 10 days, but food was refused and weight began to fall after the 6th day. By feeding the controls on the same amount of food as the experimental animals had taken the previous day, starvation glycogen values could be eliminated. There were no indications that repeated small doses of emetine impaired the liver function seriously.

To test the action of the liver in the detoxification of emetine the mortality among rats in which two-thirds of the liver had been removed and that among others not so treated, the animals being injected with the drug, was observed. Mortality was found to be higher among the hepatectomized rats, except in those which lived for more than seven days, by which time, it is said, the liver tissue had been regenerated. The authors rightly point out that the fact of an organ being concerned in the detoxification of a poison does not necessarily mean that the organ is damaged by the poison.

Lastly, to test the influence of diet on the toxicity of emetine, the drug was given to rats on six different diets, the essential principles of which are detailed in the paper. It was found that adding protein to a balanced diet did not prolong the life of the rats, although a reduction of protein lowered the animal's resistance to emetine. This reduction of resistance is ascribed to the probable impairment of hepatic function. *H. Harold Scott.*

LIEBERMANN, H. R. *Isospora hominis* **causing Acute Gastro-Enteritis in Man.** *South African Med. J.* 1945, Sept. 22, v. 19, No. 18, 341–2, 4 figs.

The patient described was a middle-aged European who had been living in a military camp in Durban for six months. A severe attack of gastro-enteritis with vomiting and diarrhoea developed one evening. This lasted for 72 hours. Bacteriological examination threw no light on the condition, which was not experienced by any other person in the same mess. Microscopical examination revealed *Entamoeba coli*, trichomonas, Charcot-Leyden crystals and red blood corpuscles as well as numerous oöcysts of *Isospora hominis*. The last named

persisted for more than 14 days, by which time all symptoms had disappeared. After the patient had returned from two weeks' sick leave they could no longer be found. It is concluded that the coccidian was the cause of the patient's illness. *C. M. Wenyon.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Lofgren, Ruth & Soule, M. H. **The Effect of Low Temperature on the Spirochetes of Relapsing Fever. I. The Viability of Four Strains of Spirochetes stored at −48 Degrees Centigrade. II. The Structure and Motility of** *Spirochaeta novyi*. *J. Bacteriology*. 1945, Sept., v. 50, No. 3, 305–11 ; 313–21, 3 figs.

The four strains used in this work, *Spirochaeta duttoni*, *S. kochi*, *S. novyi*, *S. obermeieri*, had been maintained in rats for some 40 years. During the course of infection, spirochaetes appear in the blood 24 hours after inoculation, increase rapidly up to the 4th day, and then suddenly decrease.

In the experiments, blood was taken from the heart, defibrinated by whipping, and centrifuged. The layer of spirochaetes above the red cells was mixed with the serum and distributed in 0·2 ml. amounts in Cellophane tubes. After freezing in an alcohol-carbon dioxide mixture, the tubes were stored for various lengths of time at −48°C. The organisms were then tested for infectivity by sub-inoculation into rats.

Spirochaete suspensions obtained on the 2nd day of disease remained infective for at least 27 months, whereas spirochaetes taken on the 3rd day or later became non-infective after a few days.

In a later experiment it was found that 3rd day spirochaetes were still infective after two years provided the original material consisted almost entirely of spirochaetes. The authors consider that this increased viability depends on the number of organisms in the original specimen.

A study was made of the morphology of normal forms of *Spirochaeta novyi* as compared with spirochaetes stored for seven days at −48°C., and spirochaetes which had been repeatedly frozen and thawed [the detailed descriptions cannot be summarized]. Observations on the effect of variations of temperature on motility were carried out with the help of a warming and cooling stage. The temperature of a suspension of *S. novyi* was raised to 37°C., gradually lowered to freezing point, and the cycle repeated until the organisms died. The degree of motility was noted at temperature differences of 5°C. It was found that motility diminished as the temperature fell, was abolished at zero, and was regained, but to a lessened degree, as thawing occurred. After three freezings and thawings practically all the spirochaetes were dead. *J. C. Broom.*

Wolman, B. & Wolman, M. **Studies of the Biological Properties of** *Spirochaeta recurrentis* **in the Ethiopian High Plateau.** *Ann. Trop. Med. & Parasit.* 1945, Oct. 10, v. 39, No. 2, 82–93. [27 refs.]

A description of studies on the properties of an Abyssinian strain of the spirochaete of louse-borne relapsing fever carried out at Addis Ababa, Ethiopia.

The spirochaetes were cultivated in a medium composed as follows : One cc. of egg albumin was coagulated in a sloping test-tube by heating to 80°C. To this was added about 10 cc. of a mixture of sterile human ascitic fluid 1 part, buffer solution (of *p*H 7·8) 2 parts, and saline 2 parts. The addition of 1 per

cent. glucose improved the medium. The whole was covered with 1 cc. of liquid paraffin. The prepared culture medium was heated to 56°C. for one hour on three successive days.

Spirochaetes in this culture medium were found to be able to live and multiply over a wide range of temperatures. When the cultures were kept at 0°–12°C., they remained positive after eight months of daily examination, and even at 42°–45°C. the spirochaetes remained active, though at higher temperatures they soon lost their virulence. They lived in cultures without passage up to a year, but lost their pathogenicity at an early stage.

Spirochaetes from the severe cases lived longer in cultures than those from mild cases, and first-attack spirochaetes longer than those of a second attack. The solid and fluid parts of the medium also seemed to be of different importance, and the solid part was found to harbour an invisible phase of the spirochaete. During the interval between two attacks all attempts to culture the organism from the patient's blood and bone marrow, liver, spleen and cerebrospinal fluid, were uniformly negative.

The cultures were found to exhibit a periodicity phenomenon, the spirochaetes disappearing and reappearing in the culture-tubes. The negative period ranged from 1 to 18 days, the average being about 4 days. Simultaneous cultures usually relapsed at the same time, or within a day or two of each other. There is a suggestion that the alternating immunological types also develop in cultures and that this property is independent of the antibodies of the host.

Rabbits and guineapigs were found to be naturally resistant to infection with this strain of *S. recurrentis* but could be made relatively susceptible by blocking the reticulo-endothelial system by the injection of a suspension of carbon. Both mice and monkeys were susceptible, but if the infective dose fell below about 0·5 cc. of the patient's blood, infection did not take place ; the spirochaetes, moreover, were found to be less virulent towards the end of an attack.

The Addis Ababa strain was compared with a Debra Marcos strain which differed in the severity and mortality rate of the disease it provoked. The strains behaved rather differently in experimental animals, yet the two are considered to be immunologically identical.

Lice were fed on relapsing fever patients and then kept at 37°C. and fed twice daily on the authors. Spirochaetes were continually present in the lice up to 18 days after being infected. A negative phase was not found. Neither the eggs nor the offspring of infected parents ever showed any signs of spirochaetes. Both the authors remained free from infection, thus confirming the well-known fact that the disease cannot be transmitted by the bite only of infected lice.

Relapsing fever spirochaetes were found to lose their infectivity to mice after an exposure of only 20 seconds to the ultraviolet rays of a Hanau quartz lamp at 32 cm. distance, but remained motile up to an exposure of 10 minutes.

E. Hindle.

Pirot, R. & Bourgain, M. L'infection latente résiduelle cérébrale chez le cobaye au cours des récurrentes à *Spirochaeta persica* ; la survie du spirochète dans l'encéphale est fonction de facteurs individuels. [**The Latent Residual Brain Infection in Guineapigs infected with** *Spirochaeta persica* ; **the Survival of Spirochaetes in the Brain is a Result of Individual Factors.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 1/2, 12–14.

The authors have infected guineapigs with a Persian strain of relapsing fever (*S. persica*), by the bites of *Ornithodorus* and also by direct inoculation from one animal to another. Subsequently, after varying intervals, the brains of guineapigs that had been infected were examined for residual infection by

inoculation into normal guineapigs. The results show that in some individuals spirochaetes may persist in the brain for at least 222 days, whilst in others they disappear within 45 days. Moreover, brain passage through a number of animals has no effect on the virulence of the spirochaete in guineapigs.

The authors are of the opinion that in the case of *S. persica* the localization of spirochaetes in the brain is an unpredictable phenomenon which seems to depend on the individual susceptibility of the host. *E. Hindle.*

Pirot, R. & Bourgain, M. Perte du pouvoir infectant d'*Ornithodorus tholozani* infecté congénitalement par *Spirochaeta persica* et surinfecté au stade nymphal. [**The Loss of the Infective Power of** *Ornithodorus tholozani* **Congenitally Infected with** *Spirochaeta persica* **and Superinfected in the Nymphal Stage.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 3/4, 88–90.

The authors have maintained in the laboratory a strain of *Ornithodorus tholozani* supposed to be infected with *Spirochaeta persica.* Sixty first-stage nymphs which had hatched from eggs laid by infected parents, and which proved infective, were allowed to engorge on a guineapig whose blood was swarming with *S. persica.* About 3 years later the 26 ticks, now adult, which had survived, failed to produce infection when fed on guineapigs, and a few months later the 18 survivors also gave negative results when fed on another guineapig.

The results suggest that even in the same batch of young *Ornithodorus*, all do not show the same susceptibility to infection with relapsing fever spirochaetes, and also that infected ticks seem to die out more rapidly than those which remain free from infection. (See also E. Hindle, *Parasitology*, 1911, v. 4, 133.) *E. Hindle.*

Pirot, R. & Bourgain, M. Résultats de la splénectomie chez le cobaye au cours de la récurrente à *Spirochaeta persica.* [**The Results of Splenectomy in the Guineapig on the Course of Infection with** *Spirochaeta persica.*] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 3/4, 90–93.

The authors removed the spleen from five guineapigs 55 to 149 days after inoculation with *S. persica*, when the blood had been negative for spirochaetes for considerable periods. In no case did spirochaetes reappear in the circulation.

A sixth guineapig, splenectomized whilst a few spirochaetes were still present in the blood, became negative after 7 days without showing any multiplication of the organisms. Three of the splenectomized guineapigs were reinoculated subcutaneously with *S. persica* but did not become infected, while three controls showed a heavy infection. It would appear, therefore, that, in the guineapig, removal of the spleen has no effect on the immunity following infection with *S. persica.* *E. Hindle.*

Cattan, R., Corcos, A. & Cohen, H. La forme méningée de la fièvre récurrente. [**The Meningitic Form of Relapsing Fever.**] *Bull. et Mém. Soc. Méd. Hôpit de Paris.* 1945, Nos. 21, 22 and 23, 304–6.

The authors have observed numerous cases of louse-borne relapsing fever at the Liberation Hospital, Tunis. They also mention the existence of a widespread epidemic of this disease throughout Tunisia which broke out early in 1944 and had not ended at the time of their communication (June 29, 1945).

Clinical details are given of four cases showing simple meningitic forms of

the disease, all of which readily responded to treatment with novarsenobenzol. In addition two cases are added in which it was not quite possible to dissociate the symptoms from those of a chronic intoxication.

The authors suggest an analogy between relapsing fever and leptospirosis, in both of which the liver may be affected, or meningitic symptoms develop, and in both of which relapses usually occur. In view of the importance of the meninges in the development of syphilis, meningotropism would seem to be one of the more characteristic features of human spirochaetal infections.

E. Hindle.

WOLMAN, M., OMAR, M. & ABU-TALEB, M. **Louse-borne Relapsing Fever treated with Calcium Gold Keratinate.** *Lancet.* 1945, Dec. 15, 775–7, 1 chart.

An account of the treatment of Egyptian patients infected with louse-borne relapsing fever carried out at the Imbaba Fever Hospital, Cairo.

The mortality of this epidemic averaged 2·6 per cent., but many of the patients had intercurrent diseases. A series of 160 patients whose blood contained spirochaetes and who also had pyrexia, were divided into two groups of 80 each; patients in one group were given intravenous injections of 0·5 gm. neosolganal in 5 cc. distilled water, and those in the other group were left untreated. The drug caused frequent but mild reactions, and no significant difference was found between those given 0·5 gm. neosolganal in water, and a small group of patients, not included in the above experiment, who were given 1·0 gm. neosolganal dissolved in water or calcium thiosulphate.

The injection of the drug caused the disappearance of spirochaetes within 24 hours in all cases, and in most the temperature also came down within the same period and invariably within 30 hours.

In the treated group 17·5 per cent. had relapses, and 5 per cent. non-specific rises in temperature, the corresponding figures in the control group being 65·0 and 11·2 per cent. Moreover, the mean length of interval between the attacks was significantly longer in the treated group. Three patients in the experimental group and one in the untreated group died of the infection.

[See also FELDT, this *Bulletin*, 1942, v. 39, 344.] *E. Hindle.*

HUTCHISON, J. H., PIPPARD, J. S. & GLEESON-WHITE, M. H.; SHEEHAN, H. L. **Outbreak of Weil's Disease in the British Army in Italy. Part I. Clinical Study** [HUTCHISON, PIPPARD & GLEESON-WHITE]. *Brit. Med. J.* 1946, Jan. 19, 81–3. **Part II. Post-Mortem and Histological Findings** [SHEEHAN]. *Ibid.* 83.

The description of an outbreak of Weil's disease among British soldiers in Italy who had all bathed in the River Arno, or its tributaries, and in bomb craters, during August and September, 1944. There were 17 undoubted cases, 5 fatal, all of which ran a similar course. The onset was sudden, with general weakness, shivering and high fever, nausea, and sometimes vomiting. Severe headache was common, though sometimes delayed, and general stiffness and aching developed during the next few days. The severe pain decreased when jaundice developed.

Intense conjunctival suffusion was constant and early in appearing. Icterus developed between the third and eighth days of illness and with one exception had a remarkable orange-yellow tint. The icterus persisted for weeks. Haemorrhages, varying in degree, were seen in every case; visceral bleeding was common and was a factor in the death of the five fatal cases. A striking feature common to all cases was some degree of oliguria, which in three of the fatal cases and two others became anuria for variable periods.

Treatment with penicillin, 15,000 units 3-hourly up to a total of 600,000 to 660,000 units was tried in six cases. One patient died after receiving 210,000 units, and there was no obvious effect on the course of the disease in the other five. Anti-leptospiral serum was used in three cases also without any obvious beneficial effect.

Guineapigs were inoculated with blood (5 cc.) taken from 15 cases on the 3rd to 11th days of illness and two with 10 cc. of urine from two other cases on the 13th and 16th days, respectively. Five of the animals died with typical symptoms of infection with Weil's disease and leptospirae were grown from the kidneys of three of them. The blood of 13 of the patients was examined for agglutinins against local " Cartwright " strains or stock " Wijnberg " strains and all gave positive tests at a diagnostic level of 1/300.

Convalescence was slow in each of the 12 patients who recovered and they were not fit for discharge to a convalescent depot until 17 to 20 weeks from the onset of the disease. All except one showed anaemia, which responded very slowly to iron therapy.

During the period when these men were in the wards over 1,800 cases of infective hepatitis were seen, but only rarely did this disease simulate Weil's disease, and the possibility of confusion between the two is remote. There were two doubtful cases thought to be enteric fever with jaundice until, after recovery, their blood was found to contain a rising titre of anti-leptospiral agglutinins. Non-icteric leptospirosis may also have been present among some of the milder cases of P.U.O.

After the first cases were diagnosed an embargo was placed on unauthorized bathing, etc., and the epidemic came to an end. At least two out of every ten rats caught in the neighbourhood were found to be carriers.

The post-mortem and histological findings on six cases from this epidemic, including the five referred to above, are also described. The most characteristic features were prominent lesions in the kidneys involving cast obstruction and epithelial damage in the collecting tubules and also in the second convoluted tubules, and the monocytic infiltration of the intermediate zone. There is said to be a close similarity between the appearances of the kidney in Weil's disease and in patients who died as a result of haemolytic transfusion reactions.

In every case brought to autopsy there was deep icterus of the skin and other tissues, but the liver showed no obvious abnormality, and microscopically there was never any trace of recent or healing necrosis, nor of degeneration of the hepatic cells. *E. Hindle.*

Currens, J. H. & Woodard, R. C. **Leptospirosis : Report of a Case from South Florida.** *Southern Med. J.* 1945, Dec., v. 38, No. 12, 811–13, 1 fig. [11 refs.]

Weber, R. A. & Favour, C. B. **Rat Bite Fever due to** *Streptobacillus moniliformis* **treated with Penicillin.** *Bull. Johns Hopkins Hosp.* 1945, Aug., v. 77, No. 2, 132–9, 1 chart. [15 refs.]

The record of a typical case of rat bite fever due to *Streptobacillus moniliformis* which was cultured from the blood. In order to exclude a mixed infection with *Spirillum minus* a number of white mice were inoculated with the patient's blood and remained free from infection. On the 13th day of the disease, when arthritic symptoms were at their height, penicillin in doses of 8,000 units administered intramuscularly every two hours, was started and continued for two days, followed by 6,000 units every three hours for the next ten days. Blood cultures following treatment were negative and the arthritic symptoms gradually improved and disappeared within a month after the completion of treatment.

The patient has remained without any recurrence of symptoms for more than a year. [See also this *Bulletin*, 1945, v. 42, 811.]

The growth of *Streptobacillus* from the patient's blood was found to be inhibited by as little as 0·001 unit of penicillin per cc. in media which normally supported luxuriant growth. *E. Hindle.*

LEPROSY.

CANAAN, T. **Contagiousness of Leprosy.** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*) 1945, June, v. 4, No. 6, 181–4. [12 refs.]

The author gives information regarding the incidence of leprosy in Palestine and discusses the reasons for the low degree of contagiousness of this disease, basing his remarks on 36 years' experience at the Jesus-Hilf Leprosarium. None of the seven nursing sisters who worked at the institution for 13 to 33 years contracted the disease. Only 26 per cent. of the leprosy patients admitted were known to have infected relatives, and children of lepers brought up in a separate building did not develop the disease. The author states that every case of leprosy owes the infection to direct or indirect contact with another, but that infection takes place only with difficulty owing to the low degree of virulence of Hansen's bacillus, and that new infections are rare after the age of 30 to 35 years. During the last 70–75 years the number of cases in Palestine has fallen from 220–250 to 120–150. *L. Rogers.*

DEGOTTE, J. Nouvelle contribution à l'épidémiologie de la lèpre. Étude comparative de la chefferie de Makoda 1939–1943. [**The Epidemiology of Leprosy: a Comparative Study in 1939 and 1943 in Makoda.**] *Rec. Travaux Sci. Méd Congo Belge.* 1945, July, No. 4, 70–81, 3 maps & 1 graph.

This paper reports on a comparative study of the incidence of leprosy in 1939 and 1943 in a north-western area of the Belgian Congo, the mean altitude of which is 800 metres. It consists mostly of grassland, with comparatively low leprosy incidence, and some forest areas with higher rates. In 1939, 15,526, and in 1943, 16,106 of the inhabitants were examined, and infection rates of 4·33 and 4·25 per cent., respectively, were found, indicating a slight decline in the disease. The incidence in different divisions of the area examined varied from 2 to 6 per cent. The number of new cases found in 1943 amounted to 210, the highest incidence being found in persons aged 30–40; there was also a high rate among a few persons over 60. A table is given of cases classified according to the Cairo Conference system. It is stated that the majority of the lepromatous cases have been effectively segregated, and the author deduces that the occurrence of about as many new cases in the area under observation during the four years under consideration as for leprosy in general, proves that neural leprosy is contagious. [If the segregation of the infective cases was carried out at or about 1939 the occurrence of a number of new cases during the next four years may largely be the result of infections which took place before the infective cases were segregated; the incubation, or latent, period of leprosy is often of several years' duration before the first symptoms appear.]

L. Rogers.

TROUT, C. L. **Agglutination Test with the Lepra Bacillus.** *J. Trop. Med. & Hyg.* 1945, Aug.-Sept., v. 48, No. 4, 73–4.

In this short note the results are reported of the use of an antigen prepared from cultures of a pleomorphic acid-fast bacillus obtained in California, called the Rethi bacillus, and one prepared from *Myco. leprae* separated from lepromata. One vaccine contained a toxin-filtrate taken from a milk culture of the Rethi organism, and a second a similar substance from a broth culture. Sera taken from ten persons vaccinated with these products, in 1 cc. doses weekly for six doses, agglutinated leprosy bacilli taken from lepromata. Attempts were therefore made to " immunize " the children of lepers and others who had associated with lepers, by means of these vaccines, which produced temperatures as high as 103°F. in control patients, but seldom a rise above 100°F. in lepers. The Rethi vaccines, sterilized by 1 per cent. formalin were also used for treatment in a group of lepers, and the author has the impression that the milk culture toxin-filtrate was the more effective both for treatment and prophylaxis, but it is too soon to form conclusions. *L. Rogers.*

CHORINE, V. Nouvelle réaction de floculation de la lèpre. [**A New Flocculation Reaction in Leprosy.**] *Méd. Trop.* Marseilles. 1943, Nov.-Dec., v. 3, No. 6, 419–48, 5 graphs. [13 refs.]. Also in *Ann. Inst. Pasteur.* 1944, Sept.-Oct. & Nov.–Dec., v. 70, Nos. 9/10 & 11/12, 257–76 ; 341–56, 5 graphs. [13 refs.]

These two references refer to the same paper. It gives full details of a comprehensive investigation of a flocculation reaction of diagnostic value, on the lines of the Rubino reaction, which consists in the sedimentation of formolized red corpuscles of the sheep, and of Westergren's measurements of the rapidity of sedimentation of non-formolized red corpuscles. Formolized red cells sediment more quickly than unformolized cells in the presence of the serum of a leprosy subject. Chorine has sought to isolate the active principle of formolized cells by preparing extracts of formolized blood or tissues and using the extract as an antigen. After trying a number of chemicals, he found that 90 per cent. alcohol was the best solvent of the antigen, for full details of the preparation of which the original paper should be consulted by those interested in its use.

In using this test, 1 cc. of the antigen is poured into 2 cc. of double distilled water and mixed at a speed of 200 revolutions per minute, at the end of which 8 cc. of distilled water are added. The optical density is measured by photometry and the reaction is calculated as the difference between the degree of density found for the curve of an emulsion with the serum to be tested and that of a mixture with distilled water only ; a series of tubes is put up with increasing proportions of the serum and decreasing proportions of antigen to allow curves to be plotted. A series of illustrative curves under different conditions of the numerous experiments is given in the paper, from which the following conclusions are derived. The sera to be tested should be heated for 30 minutes at 55°C. The reactions should be carried out at a temperature of 25°C. for 4 hours ; this may necessitate a cooling apparatus when working in the tropics. The antigen is best used in a dilution of 1 in 10, and within half an hour of the preparations of suspensions of it. The sera should be kept before use at a temperature of 4°C., at which they can be kept for 4 or 5 days. Three series of four tubes each are put up. In the 4 tubes of the first series, 0·15 cc. serum, in the second series 0·20, and in the third series 0·50 cc. are placed. In each of these series the first two tubes are filled up to 1 cc. with the suspension of the antigen. The remaining two tubes are filled up to 1 cc.

with alcoholized water ; these are control tubes. They are mixed well and kept at a temperature of 25°C. for four hours before the densities of the flocculation are read. The result of the reaction is obtained by subtracting the photometric degree of the control tube from that of the reaction tube.

Tables are given of the data obtained in 200 cases of leprosy and in 100 controls. A difference of over 30 in the densities between the control tubes and those showing the reaction of leprous sera is considered to be a positive reaction, for only 6 of the 100 controls gave figures up to 30–35 and 2 of 35–40. On the other hand only 10·5 per cent. of leprous sera gave figures below 30 and in 21 the figure exceeded 200. Feeble reactions indicated by figures of 30–35 numbered only 18·5 per cent., and very intense reactions of over 100 also numbered 18·5 per cent. The low reactions were chiefly met with in slightly affected or stationary cases, and in those which had much improved under treatment. High figures occurred during lepra reactions and in advanced cases with nodules. In general, tuberculoid cases gave low degrees of reaction as compared with lepromatous cases. This new reaction thus appears to be of both diagnostic and prognostic value. *L. Rogers.*

Floch, H. & de Lajudie, P. Sur la lèpre et les intradermo-réactions à la lépromine (Mitsuda) et à la lépromine (Souza-Araujo) en Guyane Française. [**The Intradermal Reactions to Lepromine and Leproline in Leprosy in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 97.* 1945, Jan., 15 pp. [24 refs.]

The authors have used both leprolin, supplied by Professor de Souza-Araujo, and lepromin, prepared by the method of Hayashi, in their tests on 86 cases of leprosy. Positive Mitsuda reactions were obtained in 90 per cent. of tuberculoid, in 51 per cent. of nerve, in 9 per cent. of mixed cases, but in none of 10 lepromatous patients. In controls not infected with leprosy, reactions were negative in those aged 8 to 9 years, but positive in four of eight persons aged 10 to 14 years. With the use of the Souza-Araujo's leprolin, similar results were obtained in lepromatous and mixed cases, but in only 27 and 23 per cent. respectively in tuberculoid and nerve cases. *L. Rogers.*

Taylor, C. E. **Leprosy of the Large Intestine and Gall-Bladder. Case Report with Review of the Literature.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Oct., v. 39, No. 2, 125–32, 5 figs. on 2 pls. [17 refs.]

The author points out that the gastrointestinal and biliary tracts are among the few parts of the body generally supposed to escape involvement in leprosy, but they now report changes in these tissues in a fatal lepromatous case in a West Indian Negro with both skin and nerve lesions. The gall-bladder showed a thickened mucosa with a mosaic pattern due to thickened patches, which, on section, revealed a few leprosy bacilli. Similarly the large intestine showed thickening of the mucous membrane, with large ulcers in the lower portions and smaller ulcers in the upper parts, in the inflamed and oedematous margins of which both scattered and clustered acid-fast lepra-like bacilli were found. The patient had died during an active lepra reaction accompanied by diarrhoea. The macroscopic and microscopic characters of the lesions are illustrated.
L. Rogers.

Montel, R. & Basset. Deux cas d'infantilisme lépreux. [**Two Cases of Leprotic Infantilism.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 11/12, 332–7, 3 figs.

FAGET, G. H. & POGGE, R. C. **The Therapeutic Effect of Promin in Leprosy.** *Pub. Health Rep.* Wash. 1945, Oct. 5, v. 60, No. 40, 1165–71, 8 figs. on 2 pls.

This paper records further trials of promin in leprosy in continuation of those reported in November 1943 [this *Bulletin*, 1944, v. 41, 494].

The present report is based on the treatment of 137 patients at the U.S.A. National Leprosarium by means of 32,000 intravenous injections amounting to a total of 126,961 gm. The average daily dose, including days of rest, varied from 0·4 gm. to 4·6 gm. The usual dosage is 1 gm. daily, increasing to 5 gm., but in some patients who showed toxic reactions the maximum daily dose did not exceed 2 gm. The present routine consists of 2 to 5 gm. daily by the intravenous route on six days each week, in courses up to two weeks with a week's rest between the courses, which allows of restoration of the red corpuscles lost during a course. The longer the duration of the treatment and the larger the doses, the greater the benefits, as shown by tables of data. The percentage of the total 137 patients treated who improved was 58·4 ; the figures for treatment of less than six months and for more than six months respectively being 25·6 and 71·4 per cent. All of six cases treated for 3 to 4 years had improved. A total dosage of less than 500 gm. only produced improvement in 25·6 per cent., but with 500 to 1,000 gm. the percentage rose to 72·5 per cent., or nearly three-fourths of the patients. Only two patients became worse while under treatment ; both were advanced cases with involvement of the larynx. The improvement was objective and not only subjective ; this is confirmed by photographs of patients with advanced lepromatous disease before and after treatment ; the benefits are not limited to action against secondary infections. In over 10 per cent. of 62 patients treated for more than one year, positive bacteriological findings have changed to negative on several consecutive monthlyexaminations. Serological reactions may also become negative coincidently with improvement in or arrest of the disease, as shown by tables of data. The cost of the drug is not given. Promin is not claimed to be a specific remedy for leprosy, but there is evidence that it has at least an inhibitory effect on the progress of the disease and that it even causes retrogression in some lesions. There is, therefore, some hope that continued chemotherapeutic research may produce a still more effective remedy. Preliminary studies suggest that diasone has a similar action to promin and that it may prove even more effective. *L. Rogers.*

GUICHARD, F. Préparation directe, en partant des graines, des esters d'*Hydnocarpus anthelmintica* Pierre, en vue du traitement de la lèpre. [**Preparation of Esters of** *H. anthelmintica*.] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 1/2, 9–12.

The author points out that most methods of preparing the soaps and ethyl esters of the fatty acids, contained in the oils used in the treatment of leprosy, are laborious, and he describes a simpler method in which the fatty acids contained in the seeds are dissolved, without transformation, in an apparatus containing absolute alcohol and sulphuric acid. The seeds are sterilized in an autoclave, and decorticated. The kernels are scorched, kept at 100°–110°C. for a night before being pulped, and are then mixed with one-third of their weight of sandstone in fine grains to facilitate the penetration of absolute alcohol to which 5 gm. sulphuric acid per 100 cc. has previously been added. The amount of acid-alcohol is equal to the weight of the pulped kernels. Some grains of pumice-stone are added and heat is applied. The results of distillation are collected over a period of ten hours. The products are treated with 15 per cent. chlorinated water several times, washed twice with distilled water and neutralized with a

small quantity of anhydrous sodium carbonate to purify the esters. To preserve them 2 gm. per cent. of anhydrous sulphate of soda is added to each full, well-corked container. Before placing in ampoules, 1 per cent. guiacol is added and the ampoules are sterilized at 115°C. for 15 minutes. The esters thus prepared keep well and are well borne by the patients. *L. Rogers.*

MONTEL, R. La méthode de Charpy dans le traitement de la lèpre. [**The Treatment of Leprosy by Charpy's Method.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 3/4, 63–4.

Charpy's method of treating lupus is as follows: vitamin D, 15 mgm. three times during the first week of treatment, twice a week during the next three weeks, and once a week during the next four months; calcium gluconate, by intravenous injection of medium doses, three times a week, and a litre of milk daily, are given for the same period. The author has tried this treatment in two cases of leprosy.

One patient, suffering from nodular leprosy and already much improved by treatment with methylene blue and chaulmoogra, showed considerable further improvement under the Charpy method; the parasitized monocytes decreased in number, the lepromata and leprous infiltrations diminished markedly in size, and the patient's bodily state improved.

The other patient, suffering from trophoneurotic leprosy, showed remarkable improvement in his general condition, increase of weight and decrease of nerve pains.

The author thinks that these results are encouraging and that further trials of the method should be made. *J. F. Corson.*

HELMINTHIASIS.

ALVES, W. & BLAIR, D. M. **Schistosomiasis: Intensive Treatment with Antimony.** *Lancet.* 1946, Jan. 5, 9–12.

In a preliminary communication one of the authors [this *Bulletin*, 1945, v. 20, 815] has already recorded the satisfactory result of rapid intensive treatment of schistosomiasis with antimony. In this paper the authors record in more detail similar treatment of 100 cases of *S. haematobium* and *S. mansoni* infections, chiefly in African soldiers. Basing their investigations on the work of CHARGIN and his collaborators (*J. Amer. Med. Ass.*, 1935, v. 104, 878) which led to the intensive arsenical therapy of syphilis with intravenous drip transfusion (HYMAN *et al.*, *ibid.*, 1939, v. 113, 1208) [see also *Bulletin of Hygiene*, 1940, v. 15, 224], and later to the therapeutically more effective "multiple syringe injections" [EAGLE and HOGAN, quoted by COLE *et al.*, *Bulletin of Hygiene*, 1944, v. 19, 194], the authors found that continuous intravenous injections of 100 cc. of a 1 per cent. solution of sodium antimonyl tartrate in 5 per cent. glucose-saline caused excruciating phlebalgia. They abandoned this technique for the multiple syringe method, giving intravenous injections three times daily at three-hour intervals for two days—a total of six injections, given at 9 a.m., 12 noon and 3 p.m. on each of two consecutive days. The preparation of antimony employed was sodium antimonyl tartrate, and the amount of drug injected at each dose was usually 1 grain or 2 grains.

Each injection was made in 10 cc. of 5 per cent. glucose-saline into a vein in the antecubital fossa and given steadily at a rate not exceeding 2 cc. per minute. At least five minutes were therefore taken for each injection, and the

authors stress the point that "*This slow and steady injection of the drug is of fundamental importance in the success of the treatment.*" In no case have toxic reactions led to interruption or discontinuance of the course, and the absence of the more troublesome manifestations usually associated with the intravenous administration of antimony was striking; cough resulted in only 16 of the 100 cases during or, more commonly, after the first injection and never lasted more than two minutes, the frequency of its occurrence diminished through the course and only two patients suffered from it as a result of their sixth and final injection. Vomiting did not occur in association with a first injection, but was encountered in six cases and two cases, respectively, with the second and third injections, and in three cases and one case, respectively, with the fifth and sixth injections. In the 100 cases, a feeling of constriction of the chest was noted by one asthmatic patient only; abdominal cramps occurred in three cases; there were no "rheumatic" pains, and no collapses. Salivation was common after the early injections, but usually vanished by the second day. The average rate and the regularity of the pulse in the whole series was not altered by the antimony dosage. In two cases there was a brisk haematuria after the third injection, but in neither did it persist. In one there was a drug rash of limited distribution appearing 24 hours after the last injection and persisting for one week. A striking feature in many cases was a state of euphoria the day after the conclusion of treatment. This could not be ascribed to relief, as the African does not as a rule fear injection treatment, and it was noticed both in Europeans and in Africans.

Data relevant to the 100 cases treated are listed in tabular form showing the species of parasite, the degree of eosinophilia, the patient's weight in pounds, and the gross dosage of S.A.T. given to each. This gross dosage ranged from 7 grains to 14 grains of S.A.T. and is based on the body weight, roughly one grain of S.A.T. being given for each 12 pounds of body weight. A man of 144 pounds would, therefore, get a gross dosage of 12 grains of S.A.T. The individual doses, six for each individual, were worked out, for the sake of economy and convenience, so that as often as possible 1 grain or 2 grains were given. For example (doses in grains) :—

	9 a.m.	12 noon	3 p.m.	9 a.m.	12 noon	3 p.m.
Patient A : gr. 10 S.A.T. given as ...	2	2	1	2	2	1
Patient B : gr. 13½ S.A.T. given as ...	2	2	2½	2½	2½	2
Patient C : gr. 9¼ S.A.T. given as ...	2	2	1	2	1¼	1

The authors record their use of an intradermal test in diagnosis. The test was performed with a cercarial antigen, and its development and application are to be described in another communication. This test was used in initial diagnosis, which was confirmed in each case by the examination of urine and of stools for schistosome ova. The skin test had become negative in a big proportion of the cases retested two months after treatment; and where this reversion took place the authors regard it as indisputable evidence of the death and dissolution of the worms. In none of the 100 cases treated were schistosome ova found in the stools or in the urine two months after treatment.

Of the 53 cases re-examined two months after treatment, only 14 gave a positive skin test. Nine of these 14 were retested one month later; six of them had then become negative; two remained positive; and one, originally strongly positive, had become only weakly positive. In no case examined two months after treatment were eggs found in the excreta.

In eight cases the urinary antimony excretion was estimated during the course of treatment and for 24 hours afterwards. Data are given in a table showing that between 70 and 80 per cent. (in the average case of this series 8 grains of S.A.T.) of the antimony injected remains in the body 72 hours after beginning treatment, and this high concentration of antimony in the body is held by the authors to be responsible for the rapid disappearance of ova and the apparent cure of all their cases.

The authors discuss the obvious economic and public health advantages inherent in their short intensive course of treatment for schistosomiasis, and point out its manifold implications in the mass treatment of the populations inhabiting the highly endemic areas of the world. They suggest that intensive antimony therapy may find a place in the treatment of kala azar, other forms of leishmaniasis and filariasis.

[This important paper may well open a new chapter in the treatment, with the heavy metals, of protozoal and of helminth infections.]

A. R. D. Adams.

MILLS, W. G. **Treatment of Schistosomiasis.** *Lancet.* 1946, Jan. 5, 12–13.

The author treated 46 cases of *S. haematobium* infestation in West African native troops with daily intramuscular injections of Stibophen (B. W. & Co.) [=Fouadin, Bayer] or of Anthiomaline (M. & B.) for 6 days during each of two successive weeks. He either "cured" or "presumably cured" all but four of the 46 cases. Where he claims cure the bladder was free from all tubercles, ulcers and granulations on monthly cystoscopy for three months after treatment. Presumably cured cases showed cystoscopically a virtually normal bladder on the occasions on which it could be examined, and no clinical relapse was reported. Toxic complications of treatment with either drug were minimal, and vanished, where present, within a week of ending treatment.

In the four uncured cases, two developed new crops of tubercles in the bladder within three months of treatment, one had a small contracted bladder and had to be invalided from the army, and the last had a severe chronic and relapsing staphylococcal cystitis which also led to his being invalided. The author draws attention to the possibility of late relapses, but considers these improbable in his series of cases. He stresses the importance of cystoscopic control throughout the treatment of urinary schistosomiasis.

A. R. D. Adams.

WARD, R. O. **Some Surgical Aspects of Urinary Bilharziasis.** *Proc. Roy. Soc. Med.* 1945, Nov., v. 39, No. 1, 27–38 (Sect. of Urology, 1–12), 23 figs. (12 coloured).

This paper, presented to the Urological Section of the Society, contains a general account of urinary schistosomiasis from the standpoint of a urological surgeon. It contains nothing new, and is designed to direct attention to the possible occurrence of schistosomiasis in members of the forces who have served overseas during the recent war. The author stresses the value of cystoscopic examination, which may reveal the diagnosis in the apparent absence of cells and of ova from the urine. *A. R. D. Adams.*

PETERS, C. N., HUNTRESS, R. L. & PORTER, J. E. **Urinary Schistosomiasis: Report of Two Cases in Maine.** *J. Urology.* 1945, Sept., v. 54, No. 3, 301–6, 3 figs.

Oliver González, J., Biaggi, N. & Rivera León, J. **The Effect of Chlorine on the Motility and Infectivity of the Cercariae of** *Schistosoma mansoni*. *Puerto Rico J. Pub. Health & Trop. Med.* 1945, Mar., v. 20, No. 3, 357–61. [Spanish version 362–6.]

The authors investigated the question as to whether the inactivity of cercariae of *S. mansoni* after exposure to chlorine (calcium hypochlorite) also implies their loss of infectivity. They found that chlorine concentrations of 1·25 to 0·5 parts per million parts of water caused the cercariae to become inactive in the average times of 2·5 to 10·4 minutes, but that a concentration of 0·2 part per million had no definite effect. In the infectivity tests, rats were exposed for one hour to the cercariae as soon as the latter were observed to be completely inactive. Concentrations of chlorine of 1·25 parts per million for a maximum duration of exposure of four minutes, or 0·44 part per million for 18 minutes made the cercariae inactive and non-infective. A concentration of 0·22 part per million did not exert a sure effect on the motility of the cercariae, and those that apparently showed inactivity at this concentration were still infective to rats.

It is suggested that a minimum period of exposure of 20 minutes to the effects of a chlorine solution yielding a minimum chlorine residual of 0·50 part per million of water, may be sufficient to render cercariae of *S. mansoni* non-infective. *J. J. C. Buckley.*

Weller, T. H. & Dammin, G. J. **The Acid-Ether Centrifugation and the Zinc Sulfate Flotation Techniques as Methods for the Recovery of the Eggs of** *Schistosoma mansoni*. *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 367–74, 1 fig. [17 refs.]

The authors carried out studies designed to evaluate and compare the effectiveness of the acid-ether centrifugation and the zinc sulphate floatation techniques in the recovery of eggs of *Schistosoma mansoni*.

Uniform suspensions were prepared of 46 faecal specimens, each containing relatively large numbers of *S. mansoni* eggs; 25 were found to contain more than 400 eggs per cc., by the Stoll count. The suspensions were employed in testing the efficiency of four different techniques. Calculations of the percentage recovery of available eggs were limited to the group of 25 suspensions containing more than 400 eggs per cc.

(1) *Acid-ether routine technique.*—One cc. of the suspension and 5 cc. of 40 per cent. HCl (40 cc. conc. HCl diluted to 100 cc.) are mixed by shaking in a 15 cc. centrifuge tube, filtered through two layers of moist gauze and then mixed with an equal quantity of ether. The mixture is shaken thoroughly and spun for 1 minute at 1,500 r.p.m. The débris floating at the acid-ether junction is loosened and then the acid and ether layers are poured off and discarded, leaving a few drops of the egg-bearing sediment which is decanted on to a slide for egg counting.

(2) *Zinc sulphate floatation with loop removal.*—Using 1 cc. of the basic suspension this method is essentially similar to that outlined by Faust *et al.* [this *Bulletin*, 1940, v. 37, 62].

(3) *Acid-ether semi-quantitative technique.*—This method follows that of (1) up to and through the centrifugation step. Thereafter the ether and acid layers, together with the floating débris, are removed by pipette and discarded leaving 1 cc. of the acid and sediment. The latter are mixed together and three samples of 0·075 cc. each are withdrawn and prepared for egg-counting. The results of six counts are averaged and the number of eggs per cc. of undiluted faeces is calculated.

(4) *Zinc sulphate semi-quantitative technique.*—Using 1 cc. of the basic suspension this technique is similar to that described by PALMER and SAWITZ [this *Bulletin*, 1942, v. 39, 98 and 771].

The results of these tests were as follows :—

(1) All 46 specimens were positive by this technique. In the group of 25 specimens containing more than 400 eggs per cc., this method gave an average recovery of 20·6 per cent. of the available eggs, with the percentage of recovery in individual specimens varying from 8 per cent. to 40 per cent.

(2) Thirty-five of the 46 specimens were positive. In the group of 25 specimens there was an average recovery of 4·6 per cent., varying from 0 per cent. to 24 per cent. in individual specimens.

(3) Forty-four of the 46 specimens were positive. In the group of 25 specimens there was an average recovery of 48·2 per cent., the range being 9 per cent. to 105 per cent.

(4) Forty-three of the 46 specimens were positive. In the group of 25 specimens there was an average recovery of 22·2 per cent., the range being 0·2 per cent. to 72 per cent.

The eggs recovered by the acid-ether technique were not distorted, but in many of the zinc sulphate preparations they showed varying degrees of shrinkage and distortion. It is concluded that the acid-ether techniques are superior to the zinc-sulphate techniques and that they appear to deserve further investigation as a routine diagnostic and survey procedure for the eggs of *S. mansoni*. *J. J. C. Buckley.*

OLIVER GONZÁLEZ, J. & PRATT, Caroline K. **Skin and Precipitin Reactions to Antigens from the Cercariae and Adults of** *Schistosoma mansoni*. *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Dec., v. 20, No. 2, 242–8, 1 fig. [Spanish version 249–56.]

Using 1 : 10,000 dilutions in both kinds of antigen, the authors found that intradermal injections with extracts of adults and cercariae of *S. mansoni* gave 100 per cent. positive results in 96 individuals who were harbouring this parasite. In a smaller group of infected individuals, dilutions of 1 : 200,000 gave positive reactions in every case, but higher dilutions than this proved negative. The skin reaction is thus characterized by a high degree of sensitivity. Non-infected controls gave no reaction though some of these were harbouring other helminths, either *Ascaris*, *Necator*, *Trichuris* or *Wuchereria*. Precipitin tests gave positive results in 93 per cent. of 86 cases, whilst all the controls were negative. The efficiency of the intradermal and precipitin test was not interfered with either by concurrent treatment with Fouadin or tartar emetic or by treatment with these drugs a considerable time previously.

The adult antigen was prepared from adult worms taken from the mesenteric veins of experimentally infected rabbits. The worms were washed several times in sterile physiological saline and then in distilled water, after which they were dried *in vacuo*. A 1 per cent. suspension of the dried and well pulverized material was made with sterile physiological saline ; this was incubated for one hour at 37°C. and left at room temperature overnight. It was then centrifuged and the clear supernatant used as a stock 1 : 100 dilution from which other dilutions were made. The cercarial antigen was made from cercariae of *S. mansoni* discharged by snails in distilled water. They were concentrated by centrifugation, washed in physiological saline and distilled water and dried *in vacuo*. A 1 per cent. suspension was then prepared in the same way as described for the adult worms.

For the skin tests, 0·1 cc. of the test antigen was injected into the volar surface of the forearm. Skin reactions considered as positive are described as

follows : within 2 to 5 minutes after injection an increase in the size of the weal could be observed. Ten minutes later it was definitely extended—sometimes with pseudopodia—and usually raised from 4 to 8 mm. It began to fade after 30 minutes. In a negative reaction there was no increase in the size or elevation of the weal and there were no pseudopodia.

In the precipitin tests, sera positive to one antigen were always positive to the other. The precipitin titres varied from 1 : 4,000 to 1 : 3,200.

J. J. C. Buckley.

Suárez, R. M. & Hernández Morales, F. **Pulmonary Schistosomiasis.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Dec., v. 20, No. 2, 194–216. [Refs. in footnotes.] [Spanish version 217–41.]

The authors review and discuss at some length the literature on the reported human cases of pulmonary involvement in schistosomiasis. They do not consider that the evidence adduced in certain of the recorded cases is adequate to substantiate the claim that the lung condition is attributable to a concurrent proven schistosome infestation elsewhere in the body, even though it may resolve on successful treatment of the schistosomiasis. They then record in very considerable [and rather superfluous] detail their laboratory and clinical findings in five cases they regard as being affected with pulmonary schistosomiasis due to *S. mansoni* infestations, demonstrated by the finding of ova in the stools. [The sputum was, apparently, not examined.] The patients were all children ranging from 11 to 15 years in age. Four of the five showed evidence of liver enlargement with cirrhosis, and all had large livers and spleens. Four showed X-ray changes in the lungs ; the X-ray reports were :—(Case 1) " pronounced peribronchial thickening, and exaggeration of normal bronchial markings, especially of right lower lobe " ; (Case 2) " atypical infiltration, more intense on right side with marked enlargement of right hilum " ; (Case 3) " enlargement of right hilum and prominence of pulmonary conus " ; (Case 4) " pronounced peribronchial thickening throughout ; fibrosis of pulmonary parenchyma of right lung with exudative type of infiltration " ; and (Case 5) " lungs negative for pleuropulmonary disease." Clinical examination of the lungs in all cases failed to reveal abnormality except in Case 4 where breath sounds were found to be " roughened at both bases "—this child had suffered from asthma. The authors consider that the first three patients suffering from " hypertension of the pulmonary circulation and parenchymatous changes in the lungs," presented a moderately advanced stage of Ayerza's syndrome, with *S. mansoni* as the aetiological agent. Each of the five children was treated with Fouadin, with subsequent disappearance of *S. mansoni* ova from the stools. The first three showed no change in the lung conditions as a result of successful treatment. In Case 4 there was " remarkable improvement in X-ray pulmonary findings " as a result of specific treatment ; while in Case 5 the asthma originally present had spontaneously ceased a year before Fouadin treatment began—suggesting it was not of schistosomal origin.

The authors point out the wide discrepancy between the X-ray and the clinical findings in the lungs of their patients, and that in only one of the five was the lung picture found to be changed after Fouadin treatment.

They conclude as follows :—

" Invasion of the lungs by schistosomiasis may produce extensive irreversible damage, if adequate treatment is not given at the proper time. Although not often encountered, this condition merits careful consideration by those physicians practising in countries where schistosomiasis mansoni exists."

[To the reviewer it is not clear on what grounds these cases are credited with pulmonary involvement directly ascribable to their schistosome infestation.]

A. R. D. Adams.

JAFFÉ, R. Observaciones sobre lesiones pulmonares producidas por *Schistosoma mansoni*. (Su frecuencia y su importancia.) [**The Frequency and Importance of Pulmonary Lesions in** *Schistosomiasis mansoni*.] *Rev. Sanidad y Asistencia Social.* Caracas. 1944, Dec., v. 9, No. 6, 1287–98. [13 refs.]

Pulmonary schistosomiasis, *i.e.* lesions due to the presence of ova of *S. mansoni* in the lungs, is far from uncommon—the author found them in 12 out of 50 cases examined—but only rarely (2 per cent. of autopsies) are the lesions extensive enough to produce changes visible to the unaided eye. SHAW & GHAREEB have noted them in 33 per cent. of cases in Egypt, and KOPPISCH in 64 per cent. of 147 examined in Porto Rico. DEW thinks that this condition is more common in infestations by *S. haematobium* than in those by *S. mansoni*.

Four questions arise from this association : (i) In what proportion of cases of schistosomiasis do we find this pulmonary involvement ? As stated above the author found it in 12 out of 50. (ii) How often are these lesions, the result of the presence of the worms or their ova, extensive enough to cause confusion with other diseases, such as tuberculosis ? This is not answered, as data are insufficient. If the nodules are few the chances of this confusion arising are slight, but if grouped, as they sometimes are, they may cause confusion unless more detailed investigation is made. (iii) Is there evidence of involvement of organs other than the lungs in these cases ? Yes, the ova may be seen in the portal radicles and the parasites and their ova in the liver and elsewhere. (iv) Is there any connexion between pulmonary schistosomiasis and tuberculosis of the lungs, in the sense that either predisposes to the other ? The author arrives at a negative conclusion, finding that tuberculosis is no more common in schistosomiasis patients than in the general population. The tubercles found in schistosomiasis do not contain any *Myco. tuberculosis* and are " pseudo-tubercles " unless the word is used purely generically.

Apart from these considerations, the lesions may be so extensive as to give rise to chronic interstitial pneumonia ; if sparse, not enough to cause any serious symptoms, but, if widespread, enough to cause secondary cardiac embarrassment [see this *Bulletin*, 1938, v. 35, 665].

In conclusion, the author is of the opinion that these pulmonary lesions of schistosomiasis have as a rule little, if any, importance, and are rarely sufficiently serious or widespread to cause symptoms, but at the same time, when radiological examination of the lungs shows small scattered nodules, the possibility of *schistosomiasis pulmonum* should be borne in mind. *H. Harold Scott.*

BANG, F., FERGUSON, M. S., HAIRSTON, N. G. & GRAHAM, O. H. **Hyperendemicity of Schistosomiasis Japonica on Leyte Island, P.I.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 407.

Ova of *Schistosoma japonicum* were found in the faeces of 80 per cent. of native children over 10 years old in the eastern side of the island of Leyte in the Philippine Islands ; as only a single examination, followed if negative by a second examination after sedimentation of a portion of the faeces, was made in each case, the authors infer that everyone in the endemic areas becomes infested before reaching the age of 15 years. The incidence was less in adults than in children, the difference being statistically significant, and this suggests that immunity may be developed. *J. F. Corson.*

MAGATH, T. B. & MATHIESON, D. R. **Infection of Wild Rats on Leyte with** *Schistosoma japonicum*. *U.S. Nav. Med. Bull.* 1945, Dec., v. 45, No. 6, 1195–202.

It is well known that the endemic area of human infestation with *Schistosoma japonicum* in Leyte Island in the Philippine Islands is limited to the

Leyte Valley, which is about 25 miles long and 8 miles wide and is situated on the east side of the island.

Wild rats in this island appear not to migrate much but to remain throughout their lives in one relatively small area ; it was thought, therefore, that an investigation of the incidence of infestation in these rats might give more information in relation to certain bodies of water and to the distribution of the snail, *Schistosomophora quadrasi*, than the examination of man and his domestic animals would, especially in the disturbed conditions caused by the war.

Rats were trapped in various localities, 163 altogether being caught ; they comprised Polynesian rats (10), Norway rats (14), and Black rats (139), the subspecies being undetermined. They were caught in the following places (the numbers infested are shown in brackets) : Tacloban, 58 (0) ; Palo, 43 (11) ; Gacao, 41 (37) ; Dagami, 7 (4) ; Santa Fé, 12 (10) ; Alanglang, 4 (2) ; San Antonio, Samar, 6 (0) ; Jinamoc Island, 2 (0) ; Total, 163 (64).

Infested rats always had eggs in the posterior central lobe of the liver, and next in frequency were the other lobes of the liver and the rectal wall ; in only two cases were eggs found in the faeces, and the authors suggest that the blood vessels of the rat's intestine are too narrow for the female worm to enter so there is insufficient pressure to force the eggs through the bowel wall.

The authors conclude that the wild rat is not important for the spread of the disease but that it might be used to define a limited area in which *S. japonicum* is being spread and that the proportions infested might indicate the intensity of infestation of other hosts in the area. *J. F. Corson.*

Johnson, A. S., Jr. & Berry, M. G. **Asiatic Schistosomiasis : Clinical Features, Sigmoidoscopic Picture and Treatment of Early Infections.** *War Medicine.* Chicago. 1945, Sept., v. 8, No. 3, 156–62, 5 figs.

Schistosoma japonicum infestation of man occurs in China, Japan, Formosa, the Celebes and the southern Philippine islands of Mindinao, Samar and Leyte. The authors record their observations on and treatment of a group of 42 cases, in the last named island, admitted to the station hospital in the early stages of the disease. In all these patients ova of *S. japonicum* were recovered from the stools, after a history of previous exposure to probably infected water. In four cases the duration of infection before the finding of eggs in the stools was determined as 30, 35, 40 and 44 days, respectively ; in the 38 others it ranged from 30 to 71 days before the manifestation of symptoms.

The authors describe in some detail the mode of onset, symptoms and signs and the investigations they made in their cases. The only constant physical sign was a tender palpable liver. Pathognomonic lesions could be seen sigmoidoscopically in 67 per cent. of their cases, and biopsy of the distinctive small yellow nodular lesions, found particularly at the recto-sigmoid junction, revealed ova. The lesions are so characteristic that routine biopsy is unnecessary.

Twenty-two patients were treated with the usual course of potassium antimonyl tartrate, and 20 with Fouadin. The former gave rise to the usual side-effects, the latter to none. The cure rates have not yet been established, but therapy resulted in clinical improvement, a fall in the average eosinophil count, and the disappearance of ova from the stools. *A. R. D. Adams.*

Larsh, J. E., Jr. **Effects of Alcohol on Natural Resistance to the Dwarf Tapeworm in Mice.** *J. Parasitology.* 1945, Oct., v. 31, No. 5, 291–300. [16 refs.]

BARNETT, L. **Progress in our Knowledge of Hydatid Disease. With some Contributions thereto from the Otago Medical School.** *New Zealand Med. J.* 1945, Dec., v. 44, No. 244, 304–8, 2 figs.

An interesting summary of work on hydatids by the Chairman of the Hydatid Research Committee. He stresses the fact, not sufficiently recognized, that primary peritoneal cysts are rare, less than 1 per cent. of the whole; they are nearly always secondary to cyst of the liver which has escaped notice, for cysts of the dome of the liver may grow slowly for 30 years or even longer before producing signs of ill-health. Also, the vast majority of primary cysts arise in childhood, and the aphorism that " a hydatid cyst is nearly as old as its host " is generally true. Biliary colic and jaundice may be caused by a cyst opening into the bile-ducts; this is not rare and, in hydatid countries, should always be borne in mind.

The author makes some observations on operative details, indicating his preference for the abdominal rather than the lower thoracic route for cysts of the dome, for these cysts are usually old and degenerated and contamination and sepsis occur twice as frequently after transthoracic as after the abdominal operation.

Lung cysts in the young should be given the chance of spontaneous cure, unless there are indications of sepsis and toxaemia. The danger of tapping is duly noted. [The abstracter had a sad experience of this more than 50 years ago, when, as house physician, he was directed to aspirate a " pleural effusion ". When the aspirator was thrust in the patient died in a few seconds, drowned in the fluid; the cyst-wall had ripped up and the lung was flooded with the fluid which autopsy showed to be hydatid.] Brain cysts, when primary, nearly always occur in childhood; if in an adult a brain cyst is probably secondary to cyst of the heart.

Study of the hexacanth embryo leads the author to conclude that the central pair of spicules is used for penetration of tissues and the lateral pairs for propulsion. The size of the embryo has been variously recorded; the author finds it to be 28μ long by 25μ broad, and the whole ovum 41 by 34μ. Again, contrary to the fairly general idea that the gastric juice of the host acts on the egg-shell to liberate the embryo, he believes (with DÉVÉ and others) that hatching takes place in the small intestine, where the contents are alkaline.

There is probably a high degree of innate immunity in dogs to hydatid infection, otherwise infection would be much more prevalent than it is; at the same time, if experiments now in hand succeed, and immunity can be artificially conferred on dogs and lambs, this will go a very long way towards the control of hydatid in the country. *H. Harold Scott.*

DESCHIENS, R. L'action anthelminthique des colorants triphénylméthaniques. [**Anthelmintic Action of Triphenylmethane Dyes.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 3/4, 111–25. [10 refs.]

DESCHIENS, R. & LAMY, L. Données expérimentales et pratiques sur les propriétés anthelminthiques de la phénothiazine (thiodiphénylamine), et de ses dérivés. [**The Anthelmintic Properties of Phenothiazine and its Derivatives.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 288–99. [22 refs.]

FLOCH, H. & DE LAJUDIE, P. Sur la filariose à *W. bancrofti* en Guyane Française, la lymphangite endémique et l'éléphantiasis des pays chauds. [**Filariasis due to *Wuchereria bancrofti* in French Guiana: Endemic Lymphangitis and Elephantiasis of the Tropics.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 109.* 1945, Aug., 17 pp. [23 refs.]

Thick blood films taken from the finger at 3 p.m. and between 9 and 10 p.m. from natives of French Guiana and others were stained with Giemsa's stain and

examined for microfilariae. These were present in 27 (12·4 per cent.) of 217 males and 20 (18·1 per cent.) of 110 females. In cases where a specific diagnosis was difficult the microfilariae were identified by measurement; all were diagnosed as of the species *Wuchereria bancrofti*. The authors have not found the embryos of *Filaria ozzardi* (*demarquayi*) or *Acanthocheilonema perstans* in natives of French Guiana.

The aetiology of tropical lymphangitis and elephantiasis is discussed and the authors subscribe to the view that they are caused by streptococcal infection.

J. F. Corson.

Rifkin, H. & Thompson, K. J. **Structural Changes in Early Filariasis.** *Arch. Pathology.* 1945, Oct., v. 40, No. 4, 220–24, 5 figs.

This account is based on a study of 30 cases. Some of the patients had been stationed in South Pacific islands where filariasis is endemic, others showed signs leading to suspicion of filarial infestation. Eighteen of them had blood eosinophilia of 6–11 per cent., in others the percentage did not exceed the normal and the total red and white counts were within normal limits. No organisms, such as streptococci, were found in any of the lesions. In most, the first symptoms were a painful, enlarged lymph node, a brawny lymphangitis, or an acute epididymo-funiculitis. In 12 the genitalia or lower limbs were primarily involved; in 9 the upper limb, and in 9 the upper and lower limbs at the same time. Presence of the filaria was demonstrated in 6 of the patients; in the others, though the worms were not found, the histological picture was to all intents and purposes the same.

The essential changes comprised marked hyperplasia of the related lymph follicles, with mitotic figures at the germinal centres, and general infiltration with eosinophilia. The lymphatic channels showed "fluid lakes" of thin pink-staining albuminoid fluid. The histological changes were dilatation of the lumen of the lymphatics with necrotic débris, thickening of the wall, and eosinophilic infiltration, with epithelioid cells, fibroblasts and multinucleated cells of the Langhans type. Three cases are detailed—in men of 23, 25 and 29 years respectively—and a plate of six photomicrographs illustrates these changes so far as uncoloured photographs can do so.

The author summarizes the changes in these words: "There appear to be three stages in the genesis of filariasis [*i.e.* the local tissue reaction to infestation] first, the acute stage, manifested by a typical allergic reaction, which may be local or systemic; second, the subacute or early chronic stage, characterized by the development of a proliferative granulation tissue and occurring in lymphatic tissues harboring the parasite; third, the late chronic stage of the disease, typified by a non-specific fibrous tissue overgrowth. As in all classifications, no distinct delineation is possible. One stage merges imperceptibly into the other."

It is noteworthy that a large proportion of the patients became infested without presenting any symptoms, at all events any at present recognizable.

H. Harold Scott.

Dhayagude, R. G. **Microfilarial Granuloma of the Spleen: Observations in Twelve Additional Cases.** *Arch. Pathology.* 1945, Oct., v. 40, No. 4, 275–8, 8 figs. on 1 pl.

This article may be regarded as confirmatory, or supplementary, to that published in 1942 by the author and B. M. Amin on the same subject [see this *Bulletin*, 1942, v. 39, 707], in which 11 such cases are considered. The present record brings the total to 23. Taking all together, the ages of the subjects ranged from 6 to 70 years, but 20 were between 25 and 50 years; 5 were females,

18 were males. In 10 of the present series, however, *living* specimens of microfilariae were obtained from the splenic granulomata, whereas in the previous 11, the description was made from fixed tissues. Obtaining them alive has enabled a definite diagnosis of *W. bancrofti* to be made. Prior to this there had been a suspicion that it might be the Malayan filaria. Even when microfilariae are not seen the histological structure is the same (except that the lymphocytes, eosinophiles and giant cells of early granulomatous reaction had disappeared) and represented a later fibrosed condition of a granulomatous lesion. The macroscopic features, the author avers, are so definite that mere inspection enables one to say that the lesion is of microfilarial genesis.

H. Harold Scott.

See also p. 295, COGGESHALL, L. T. **Malaria and Filariasis in the Returning Serviceman.**

CULBERTSON, J. T., ROSE, H. M. & OLIVER-GONZALEZ, J. **The Chemotherapy of Human Filariasis by the Administration of Neostibosan. Second Report.** *Amer. J. Trop. Med.* 1945, Sept., v. 25, No. 5, 403–6.

Bancroftian filariasis, although it has proved a smaller military problem than was expected, is widespread in the native populations of certain areas. Measures of protection adequate for military personnel are inadequate for civilian communities. A satisfactory and specific treatment of the infected would constitute a significant step in solving the practical problem of human filariasis.

The authors have already published one report on the use of neostibosan as a therapeutic agent in this infection [this *Bulletin*, 1946, v. 43, 54]; the present paper constitutes a second report on the progress of the cases therein recorded, twelve months after the end of treatment. Data are given, in two tables, of the 30 native Porto Ricans infected with *Wuchereria bancrofti*, and treated with neostibosan, and of the 15 untreated controls similarly infected.

The treated cases received three intravenous injections of neostibosan on alternate days, the first being 50 mgm., the second 100 mgm. or 150 mgm., and the third 300 mgm. of the drug. Thereafter 300 mgm. were given daily or on alternate days for 33 or 48 days. The microfilariae were counted in 60 cmm. of dried and stained nocturnal finger blood at least monthly for 9 to 14 months after treatment.

The authors give the following summary :—

" Thirty patients infected with *Wuchereria bancrofti* were treated with neostibosan for from 33 to 48 days. After twelve months, 13 of the patients were free of circulating microfilariae and 5 others had lost from 87 to 99 per cent. of their embryos, compared with the number in the blood before treatment. The twelve remaining patients showed little promise of eventual eradication of their infections after observation for nine months.

" Of 15 control untreated patients infected with *Wuchereria bancrofti*, all remained infected for 14 months of observation. In this interval, 12 showed an over-all increase and 3 showed a decrease in the number of circulating microfilariae.

" Among the treated patients, some of whom had been free of microfilariae for 12 months, none presented untoward symptoms referable to treatment."

A. R. D. Adams.

MARILL, F. G. & ALCAY, L. Modifications hématologiques chez des noirs sénégalais atteints d'onchocercose cutanée (gale filarienne). [**Blood Changes in Senegalese Infected with** *O. volvulus*.] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 5/6, 132–6.

TISSEUIL, J. Troubles de la vue et onchocercose cutanée au Sénégal. [**Eye Disease and Onchocerciasis in Senegal.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 311–12.

HUMMELEN, L. R. Helminthiasis bij kinderen in het bizonder binnen het schoolartsendistrict "Huizen". [**Helminthiasis in Children, particularly in the School Medical Officer's District of Huizen.**] [Thesis for Doctorate of Medicine, University of Amsterdam, 30 Nov., 1945.] 86 pp., 1 pl. [Numerous refs.] English summary 87–91. 1945. Zutphen: J. B. van den Brink & Co.

The author examined the faeces of 1,708 schoolchildren in towns and villages of the district of Huizen to the south-east of Amsterdam for worm eggs; there were about equal numbers of children of each sex. Ova of *Ascaris lumbricoides* were found in 14·6 per cent., of *Trichuris trichiura* in 12·2 per cent., and of both species in 4·9 per cent.; altogether 22 per cent. of the children showed helminth infestation. In different places *Ascaris* infestation varied from 0·9 to 48·7 per cent., *Trichuris* from 2·9 to 38·8 per cent., and double infestation from 0 to 17 per cent.; altogether the percentage varied from 0 to 52·7. Ova of *Taenia* and *Ancylostoma* were not found.

In addition, a similar examination was made of 100 schoolchildren of Amsterdam and of 104 of West-Terschelling; in the former the figures for *Ascaris* and *Trichuris* were 0 and 3 per cent. respectively and in the latter they were 35 and 84 per cent., respectively.

The degree of infestation depended on the state of local hygiene; it was greater in the poorer classes and in rural than in urban communities. It was found that vegetables grown for food were manured with human faeces.

Few symptoms were caused and body weight was not affected nor, apparently, was the intelligence of the children.

The faeces of the same 1,912 children were also examined for ova of *Enterobius*; in different localities the rate of infestation varied from 3 to 26·1 per cent., average 10·5; a further examination of 1,060 children was made with the glass pestle method of SCHÜFFNER and SWELLENGREBEL [this *Bulletin*, 1945, v. 42, 922] and rates of infestation varying from 72 to 100 per cent., average 85·2, were found. The high percentage of *Enterobius* infestation is considered to be due to reinfestation.

The author considered that the schools did not play a part in the spread of *Ascaris* and *Trichuris* infestation but that they did in the case of *Enterobius*; eggs of the last species were found in the dust of a sanatorium.

Fifty-five children infested with *Enterobius* were treated with gentian violet—5 mgm. for each year of age three times a day for a week, then a week's interval, and then the same dosage repeated for another week. The rate of infestation was reduced to about half, but after 8 weeks it had again risen to 98 per cent. The author does not recommend mass treatment of schoolchildren with the anthelmintics at present available. *J. F. Corson.*

MCNAUGHT, J. B. **Laboratory Procedures for the Diagnosis of Trichinosis.** *Amer. J. Clin. Path.* 1944, Sept., v. 14, No. 9, Tech. Sect. 87–93, 3 figs. [18 refs.]

SWELLENGREBEL, N. H. & SCHÜFFNER, W. A. P. Een methode ter opsporing van besmetting met Oxyuris vermicularis. [**A Method of Diagnosis of *Enterobius* Infection.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1943, Aug. 21 & 28, v. 87, Nos. 34/35, 1363–6, 3 figs.

See this *Bulletin*, 1945, v. 42, 922.

Bijlmer, J. Een uitzonderlijk geval van oxyuriasis van den darmwand. [**An Unusual Case of *Enterobius* Infection of the Bowel Wall.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1944, Jan. 1 & 8, v. 88, No. 1/2, 24–6, 10 figs. on 2 pls.

Guilhon, J. Essais de traitement des oxyuroses par la thiodiphénylamine. [**The Treatment of *Enterobius* Infections with Phenothiazine.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 9/10, 279–86.

Pepper, O. H. P. & Díaz Rivera, R. S. **Trichiniasis. A Review of the Clinical Picture and Laboratory Diagnosis of the Disease, with an Analysis of several Cases.** *Puerto Rico J. Pub. Health & Trop. Med.* 1945, Mar., v. 20, No. 3, 367–76. [Refs. in footnotes.] [Spanish version 377–88.]

In this useful brief survey of trichiniasis the authors bring out well the variety of the possible symptoms and the difficulty which may be encountered in diagnosis. Most of the information given is available in textbooks. After a survey of the American and Spanish literature, the authors are impressed by the " tremendously high incidence " of trichiniasis recorded in some countries of temperate zones in comparison with the tropics, where trichiniasis seems to be relatively rare. They are unable to account for this difference, but suggest that it may be due to the greater efficiency of investigation done in the United States and to differences in diet. In the tropics people are so poor that they eat less meat and more carbohydrate and they cook their food more thoroughly (especially those of Spanish descent). Also when diarrhoea and eosinophilia occur together in the tropics they may be ascribed to intestinal parasites without examination for *Trichinella* being made. The apparently low incidence of trichiniasis in the tropics should be investigated further. The authors remark upon the fact that trichiniasis has not yet been recorded from Porto Rico, although large quantities of pork products are eaten there and most of these are imported from the United States, where Dickman [*Bulletin of Hygiene*, 1938, v. 13, 729] found, in Philadelphia, *Trichinella* in 10 per cent. of pork sausage picked at random in the meat markets. The incidence of trichiniasis in the United States, determined by post-mortem examinations, is 10 to 25 per cent.

The brief description of the clinical picture emphasizes the great variety of symptoms which may be encountered [see also recent abstracts in this *Bulletin*]. The diseases simulated include meningitis, poliomyelitis, encephalitis, polyneuritis, periarteritis nodosa, tetanus (when the masticatory muscles are involved), typhoid fever, scarlet fever, German measles and *erythema multiforme*. The authors make the somewhat unorthodox statement that the diaphragm and muscles of the thoracic and abdominal walls are less frequently involved than the gastrocnemii, deltoid, biceps and muscles of the eye. For diagnosis they rely upon demonstration of the larvae in the blood, cerebrospinal fluid and muscles and they regard eosinophilia as of great diagnostic value. They demonstrate the larvae in the blood (during the early invasion period) by diluting 5 to 10 cc. of venous blood with 2 per cent. acetic acid and examining the sediment. The cerebrospinal fluid is centrifuged and the deposit examined [*cf.* Gaase, this *Bulletin*, 1945, v. 42, 481, for the presence of antibodies in the cerebrospinal fluid]. Eosinophilia is not a measure of the severity of trichiniasis, because it may be very low in the more acute cases [*cf.* Gaase, this *Bulletin*, 1946, v. 43, 236]. It is a drawback of the precipitin test that it does not become positive until the fourth week. Discussing the limitations of the Bachman intradermal test, the authors say that it sometimes fails in cases of

proved trichiniasis, and that in others the reaction is delayed ; group reactions with other parasites occur and some normal people may give false positives [*cf.* recent abstracts in this *Bulletin*].

The authors record brief details of eight subjects. The first shows the simulation by trichiniasis of an acute abdominal emergency ; the second, its simulation of nephritis and tetanus ; the third, involvement of the eyes and their muscles ; the fourth, the infestation of four youths from the same source (pork) ; the fifth, myocardial damage ; the sixth, extreme myositis ; the seventh, the possible association of trichiniasis with angioneurotic oedema ; and the eighth its co-existence with asthma. *G. Lapage.*

Oliver González, J. Diferencias antigénicas entre la larva y el adulto de la *Trichinella spiralis*. [**Antigenic Differences between the Larva and Adult of** *Trichinella spiralis*.] *Puerto Rico J. Pub. Health & Trop. Med.* 1945, Mar., v. 20, No. 3, 389–416, 1 fig. [Refs. in footnotes.]

This is a translation of the author's earlier paper (*J. Infect. Dis.*, 1941, v. 69, 254) [noted by title only in this *Bulletin*, 1942, v. 39, 627]. Only the author's main conclusions can be given here ; some of them have already been mentioned in this *Bulletin*, 1944, v. 41, 225. The author summarizes in the paper under review and in earlier papers [this *Bulletin*, 1941, v. 38, 528], the history of the discovery that, when some animals acquire resistance, either naturally or by artificial infestation, to certain metazoan parasites and, when the living larvae of the parasites concerned (and also the adults of *Trichinella spiralis*) are put into the immune sera thus produced, granular precipitates are formed around the external openings of these larvae (mouth, anus and sometimes the vulva). The immune sera also have, in some instances, a parasiticidal action which causes the death and disintegration of the larvae. Precipitates are also deposited in the immune serum.

[Blacklock, Gordon and Fine (this *Bulletin*, 1930, v. 27, 880) noted that these precipitates occur in the gut and round the extremities of the larvae of the dipterous insect *Cordylobia anthropophaga*, which causes myiasis. They have been since observed around the mouth and sometimes also around the anus and vulva of larvae of the nematodes *Nippostrongylus muris*, *Ancylostoma caninum*, *Trichinella spiralis*, *Strongyloides ratti* and *Ascaris lumbricoides* (see Oliver González, this *Bulletin*, 1944, v. 41, 223.)]

As a result of his studies of this effect of immune sera of rabbits upon the larvae of *Trichinella spiralis*, González believes that these precipitates are formed when the secretions and excretions of the larvae or the adults of this species come into contact with antibodies in the immune serum. In this paper he records his conclusion that two types of antibody, one antilarval and the other antiadult, appear in the serum of rabbits experimentally parasitized by *Trichinella spiralis*, and that these have a specific action against the larvae and adults respectively. He suggests that there may be also a third protective antibody, inseparable from the antiadult antibody, that this nematode may possess, at each phase of its development, several antigens and that those studied in this paper are only some of those present.

The antiadult antibody causes *in vitro* (in hanging drops) the formation of precipitates around the mouth, anus and vulva of the adult *Trichinella*. The oral precipitate is much the most frequent and appears very quickly. The death of the larvae may result (see below). The antiadult antibody can be detected *in vitro* at the end of about 15 days after the infestation ; its action increases moderately between the 25th and 35th days and begins to decrease until it ceases on the 50th day. It reappears in full activity on the 5th day

after superinfestation, rising abruptly then, reaching its maximum and continuing to increase when infestations are repeated. It then confers on rats a partial immunity against the intestinal phase of the infestation, and passive immunity can be transferred from rabbits to rats.

The antilarval antibody provokes, *in vitro*, precipitates around the mouth, but not at the anus, of the larva. It appears in the serum on about the 30th day after infestation and attains its maximum action between the 45th and 60th days. Its concentration does not increase, but remains moderately high during repeated infestations, but it gives hardly any passive immunity to rats. The author therefore suggests that it is the antiadult antibody which is the decisive factor in the transference of passive immunity from one animal to another (*e.g.* rabbits to rats). For his reasons for this conclusion the paper itself must be consulted.

The antiadult and antilarval antigens described in this paper probably constitute, the author thinks, complete groups of antigens which, acting as groups, provoke reactions which are qualitatively different, the differences probably depending on the relative proportions in which the various antigens are present and also on the appearance of new antigens as developmental stages succeed one another. The author claims that Table I shows that the antiadult antibody, but not the antilarval, is active against immature larvae at the moment when they leave the uterus. This suggests, the author thinks, that immature larvae have an antigenic structure similar to that of the adults. His studies suggest that this antigenic structure begins to develop when the larvae are 20 days old. As the larvae mature, new antigenic structures are developed. These antigenic differences may possibly depend upon the fact that the developing embryos and the adults feed upon the intestinal wall, while the mature larvae feed upon red muscle. In other words the antigenicity of the parasite may be related to the enzyme activity of the special tissue which it parasitizes. The differences observed between the different antigens may perhaps be similar to those shown by some lactobacilli which, by fermenting sugars, produce changes in their polysaccharide antigens [see MELCHER, this *Bulletin*, 1944, v. 41, 225].

González discusses his results in relation to certain general problems of immunity to helminth infestations. He compares his results with those of CAMPBELL (*J. Immunology*, 1938, v. 35, 465), who found that in rats infested with the larval stages of *Taenia taeniaeformis*, two types of antibodies appeared, one produced in the first week of the infestation and able to destroy unencysted larval stages of this tapeworm, the other produced when the infestation was established and able to destroy encysted larval stages. González also discusses the work of TALIAFERRO [this *Bulletin*, 1940, v. 37, 887 ; 1941, v. 38, 110] on the inability of certain antigens to saturate antibodies. González gives the following possible explanations of the failure of some observers to transfer passive immunity to *Trichinella spiralis* or to observe any deleterious action of immune sera *in vitro* : (1) the sera used for transfer of passive immunity were mo tly obtained by these observers from animals which had been artificially infested only once ; and the sera were taken a long time after infestation, or perhaps at the moment when the antiadult antibody was very scarce in the serum ; (2) some observers have used the sera of rats and guineapigs, which produce, González thinks, antibodies much less powerful than those produced in rabbit serum ; (3) observations on the deleterious action *in vitro* have been made for 24 hours only, which is a very short time for their observation ; González made observations for as long as 7 days ; (4) the movements of the larvae may have dispersed the precipitates in some instances, especially when they have not been given sufficient space in the apparatus used. MCCOY [this *Bulletin*, 1941, v. 38, 529] suggested that resistance to *Trichinella spiralis* is

chiefly mechanical, the adults being expelled as the result of peristalsis and secretion by the intestinal mucosa of increasing quantities of mucus ; he doubted the existence of humoral resistance to them. CHANDLER (*Amer. J. Trop. Med.*, 1939, v. 19, 309) postulated the existence of a local (intestinal) resistance provoked by antibodies which do not get into the blood in appreciable quantities but are absorbed and retained by certain cells of the intestinal mucosa ; he thought that this type of resistance may be the most important one in trichiniasis and that the other type of resistance is produced when parasites migrate and liberate antigen into the circulation, so that antibodies are produced there. TALIAFERRO [this *Bulletin*, 1934, v. 31, 818] believes that the so-called parenteral and intestinal immunity are fundamentally the same and are produced by the same mechanism. As TALIAFERRO and SARLES (*J. Infect. Dis.*, 1939, v. 64, 157) have pointed out, *Trichinella spiralis* (and *Nippostrongylus muris*) penetrate into the epithelium of the gut and thus impregnate with their secretions and excretions the fluids of the intestinal wall, so that infestations with species which do this are in reality parenteral. The existence of an intestinal immunity in the absence or lack of increase of precipitins in the blood, demonstrated by BACHMAN and RODRÍGUEZ MOLINA (*Amer. J. Hyg.*, 1933, v. 18, 266) and confirmed by CHANDLER [this *Bulletin*, 1940, v. 37, 216] and by González (see the present paper) is due, González thinks, to the fact that the above workers used an antilarval and not an antiadult antigen. The view that antibodies do participate in the intestinal phase of the immunity to *Trichinella spiralis* is reinforced by the fact, which has, González claims, been perfectly proved, that the antiadult antibodies increase positively as the infestations are repeated [see also ROTH, this *Bulletin*, 1944, v. 41, 59]. *G. Lapage.*

ROTH, H. **Serodiagnosis of Trichinosis by Microscopical Testing with Living *Trichina* Larvae.** *Nature*, 1945, June 23, 758–9, 1 fig.

Roth (*Acta. Path. et Microbiol. Scandinavica*, 1941, v. 18, 160) described a method of using, for the diagnosis of trichiniasis, the fact that, when living larvae of *Trichinella spiralis* are placed in the serum of animals immunized against this species (immune serum), granular precipitates are formed round the external openings of the larvae and in the serum [see also GONZÁLEZ above and other recent abstracts in this *Bulletin*]. This method has, since 1941, been used in Denmark and Sweden by Roth and in Norway by HAUGE (*Norsk. Vet. Tidsskr.*, 1944, v. 56, 364). BERGWALL (*Svenska Läkartidn.*, 1943, v. 40, 72) and NORUP (*ibid.*, 1944, v. 41, 2420) have also reported on it. There have been, during recent years, several outbreaks of trichiniasis in Norway and Sweden, but none in Denmark or Finland.

The test is done as follows : Larvae are obtained by artificial digestion of trichinized muscle and washed in sterile saline. For each test about 100 sterile larvae are put into the hollow of a sterile thick hollow-ground slide and covered with 0·5 cc. of immune serum which has been centrifuged twice. A sterile coverslip excludes all air bubbles. The slides are then placed in a moist chamber (made by placing wet blotting paper in a glass dish and covering this with wire netting) and incubated at 37°C. They are examined after 5 hours and again after 24 hours [contrast GONZÁLEZ in the abstract above, who regards 24 hours as too short a time]. If the serum contains antibodies, bubble-like or finely granular precipitates are seen, mostly around the anterior ends of the larvae. After 24 hours the precipitates are chiefly seen in the serum. The amount and form of the precipitates vary greatly and depend largely on the age and size of the infestation. The reaction usually becomes positive between the 10th and the 20th day after the first appearance of symptoms, but in a few instances a faint reaction was obtained before the 10th day. The commonest

first symptoms are fever and oedema of the eyelids. From mild cases the antibodies seem to disappear about a year after recovery from the disease. Roth diagnosed 80 subjects in this way and could exclude trichiniasis from the differential diagnosis of 30 others in whom trichiniasis had been suspected. The test was, Roth considers, more sensitive and more specific than the intradermal or precipitin tests. [The author does not give details of his cases in support of this conclusion.] " Similar reliable results " were obtained when the test was applied to pigs (which were positive 17 days after infestation), dogs, cats, silver foxes and guineapigs. *G. Lapage.*

SUESSENGUTH, Hazel & KLINE, B. S. **A Simple Rapid Flocculation Slide Test for Trichinosis in Man and in Swine.** *Amer. J. Clin. Path.* 1944, Sept., v. 14, No. 9, 471–84, 1 fig. & 4 charts. [44 refs.]

The authors describe a flocculation slide test (also outlined by MCNAUGHT, below) for the diagnosis of trichiniasis in man and in pigs which can be done in " less than ten minutes " and is, they claim, simple, sensitive and specific.

The test is a development of Suessenguth's observation that an alkaline aqueous extract of powdered *Trichinella* larvae has the power of coating cholesterin crystals and of acting as a specific and sensitive antigen in a flocculation slide test. It is suggested that extracts of other injurious agents may act in a similar way and provide antigens for similar flocculation slide tests.

The materials used are essentially the same as those used for the flocculation slide test for the diagnosis of syphilis devised by KLINE (*J. Lab. & Clin. Med.*, 1930, v. 16, 186) [see also *Bulletin of Hyg.*, 1930, v. 5, 87 ; 1931, v. 6, 174 & 692]. The antigen used is an alkaline aqueous extract of *Trichinella* larvae. Larvae isolated by digestion from trichinized rat muscle are recovered by the modification of the Baermann apparatus devised for this purpose by HOBMAIER and MEYER (*Science*, 1937, Dec. 17, 568). The larvae are then dried in a vacuum desiccator over sulphuric acid for 24 hours and ground up in a glass mortar to a very fine powder. This powder is then extracted with 4·8 per cent. sodium carbonate solution. From this extract an antigen emulsion is prepared by placing 0·43 cc. of distilled water in a one-ounce bottle and allowing 0·5 cc. of 1 per cent. cholesterol (Pfanstiehl C.P. precipitated from alcohol for Kline tests) solution in absolute alcohol to fall drop by drop into the bottle. After rotation of the bottle for 20 seconds on a flat surface, 0·15 cc. of antigen is pipetted into it and the bottle is shaken for 1 minute. Then 1·12 cc. of 0·85 per cent. sodium chloride solution is rapidly run in and the bottle is again shaken for one minute. The emulsion thus obtained is refrigerated overnight and is then ready for use. It retains a satisfactory sensitivity and specificity for 6 weeks if it is kept tightly corked and in the refrigerator. The crystals of cholesterol should then be very small, uniform in size and completely dispersed. If they are not dispersed because the antigen had not coated them, another 0·15 cc. of antigen emulsion is added and the bottle is again shaken. Any flaky material found after refrigeration overnight is removed by centrifuging.

The test is done by first heating the serum to be tested to 56°C. for 30 minutes or to 61° to 63°C. for 4 minutes and then pipetting 0·05 cc. of it into the kind of paraffin-ringed slide used for the flocculation slide test for the diagnosis of syphilis. Twelve sera can be tested at one time. One small drop of the antigen emulsion is allowed to fall into the serum from a Wright pipette or from a syringe with a 26-gauge needle. The slide is then rotated on a flat surface for 4 minutes through a circle three-quarters of an inch in diameter at the rate of 150 rotations per minute. Faster rotation reduces the sensitivity of the test. The result is then read at once through a microscope at a magnification of $\times 100$. If the reaction is *negative*, the crystals of cholesterol coated with the antigen are completely dispersed and there is no clumping.

In flocculation tests, coarse, microscopically visible antigen particles require much less antigen to alter their surfaces than is required by those present in the fine dispersions of precipitation (see EAGLE, *Bulletin of Hyg.*, 1931, v. 6, 375 ; KLINE, *J. Lab. & Clin. Med.*, 1931, v. 16, 1202, and ZINSSER, *J. Immunology*, 1930, v. 18, 483). In the precipitin test the titre is determined by using dilutions of the antigen solution and an optimal amount of undiluted serum ; in the flocculation test the titre is determined by using progressive dilution of the serum and an optimal amount of antigen emulsion and it is truly a measure of the antigen content of the serum. The use of the paraffin-ringed slides, and rotation, accelerate the reaction.

Positive flocculation reactions of the type here described were obtained by the authors with the sera of 14 human subjects. In 13 of these trichiniasis was also diagnosed by clinical evidence ; biopsy was positive in 9 and negative in one of these 13 and on 3 of them it was not done. One subject, not diagnosed clinically, gave a positive flocculation test and a negative biopsy ; the authors suggest that this may have been a false positive.

Negative flocculation reactions were shown by 882 human subjects. Among these : (*a*) 857 showed no clinical evidence of trichiniasis ; three of these 857 were infested wfth *Ascaris*, *Echinococcus* and *Entamoeba histolytica* respectively, and 140 gave positive flocculation reactions for syphilis ; no biopsies were done on these 857 subjects ; (*b*) 24 showed some clinical evidence of trichiniasis ; two of these gave negative biopsies ; on the remaining 22 biopsy was not done ; (*c*) one subject showed clinical evidence of trichiniasis but gave a negative flocculation reaction ; unspecified " parasites " had, however, been found earlier in the stools of this man and presumably these were *Trichinella*, because the authors suggest that the flocculation test on him was a false negative test. Study of the sera of three human subjects which gave positive reactions showed that one was positive from the 21st to the 33rd day after infestation, the second was positive on the 54th day but became negative 10 months after infestation, while the third was, like the sera of pigs tested [see below], positive 10 months after infestation. [This persistence of the positive reaction in both human and pig sera and also the fact that the test is apparently specific enough to differentiate between syphilis and trichiniasis and between trichiniasis and infestation with some other intestinal parasites, seem to be valuable features.]

The value of the test for the diagnosis of trichiniasis in swine was studied by testing the sera of slaughter-house hogs and pigs experimentally infested by feeding them with trichinized rat muscle. Negative flocculation tests were given by the sera of 169 pigs. Of these 157 were slaughter-house hogs; 12 were tested before their experimental infestation; these 12 gave negative flocculation reactions for longer than two weeks after infestation. Even the pig which showed the heaviest infestation, from which it died in 16 days, gave a negative flocculation test up to the day of its death.

Positive flocculation tests were given by the sera of eleven experimentally infested swine. The test first became positive (± to ++++) in all these at about 2 to 4 weeks after infestation and remained positive for 10 months after. The highest titre in swine sera was 1 : 64, the lowest 1 : 16. The highest titre in man was 1 : 128 [the lowest is not stated]. The earliest peak of antibody in pig serum was found on the 23rd day and the latest on the 55th day. Eleven biopsies were done on the pigs at times varying from 16 days to 7¾ months after infestation. Study of the degeneration and necrosis observed around the larvae in the pig muscle suggested that the larvae were maintaining themselves by destroying muscle cells " long after " they had been encapsulated.

The authors state that, in the average case, the flocculation reaction does not become positive until about 3 weeks after infestation. The first positive

reaction in both man and swine was obtained between the 14th and 17th days, and the 25th and 27th days. Because the average life of swine fed for the market is about one year and because the reaction may remain positive for 10 months after infestation, this simple test is, the authors claim, a valuable means of testing swine and therefore of preventing human trichiniasis. It involves no disturbance of normal slaughter-house procedures and a number of pig sera can be tested by one man in a few minutes.

The authors give a valuable summary of the literature dealing with serological tests for the diagnoses of trichiniasis. *G. Lapage.*

GOULD, S. E. **A New Type of Trichinoscope.** *Amer. J. Clin. Path.* 1944, Sept., v. 14, No. 9, Tech. Sect. 98–100, 2 figs.

The author has devised a ring-shaped trichinoscope. The advantages claimed for it are that it is more easily and cheaply made than other types (see, for example, MCNAUGHT, below) and is stronger and gives a uniform compression of muscle.

It consists of two circular glass plates with a diameter of 11–5 cm. and a thickness of 3·3 mm., with ground edges. The top surface of the bottom plate may be ruled with parallel lines at intervals of 1·1 cm. These glass plates are held in flat metal rings which have an outer diameter of 13·4 cm. and an inner diameter of 10·8 cm. The outer 8 mm. of the width of each metal ring is 4 mm. thick ; the inner 5 mm. of the width of both of them is, however, counterbored to a thickness of 2 mm. The glass plates are thus held in position in a shallower (counterbored) space between the two rings. The metal rings may be chromium-plated. Compression of muscle placed between the glass plates is applied by means of two winged screws set at opposite sides of the rings, which screw down upon bolts fixed to the lower metal ring. Photographs of the trichinoscope show both its separate parts and the assembled instrument.

G. Lapage.

MCNAUGHT, J. B. **Laboratory Procedures for the Diagnosis of Trichinosis.** *Amer. J. Clin. Path.* 1944, Sept., v. 14, No. 9, Tech. Sect. 87–93, 3 figs. [18 refs.]

DEFICIENCY DISEASES.

PLATT, B. S. **Tables of Representative Values of Foods commonly used in Tropical Countries.** *Med. Res. Council. Spec. Rep. Ser. No. 253.* 41 pp. [Numerous refs.] 1945. London : H.M. Stationery Office. [9*d.*] [Summary appears also in *Bulletin of Hygiene.*]

Tables of the nutritive value of foods are a basic need in any surveys of nutrition, and there is wide demand for such a publication as this for use in tropical countries. The values given here are obtained partly from an extensive survey of the literature and partly from analyses of samples collected by the Nyasaland Nutrition Survey. An attempt has been made to assess the weight to be attached to the various analyses, and to arrive at representative values for a suitable range of foodstuffs. These values are considered to be sufficiently well founded for the purpose for which they have been compiled, namely, the evaluation of dietary data based on records of group intake. They are not suitable for surveys by the individual method, nor for precise nutritional investigations in individual human and animal subjects.

Figures are given for 233 foodstuffs representative of the dietary commonly found in tropical countries. Values given refer to the portion usually eaten, and, where possible, a figure for wastage is shown as a percentage of the food as purchased. The water content is given as accurately as possible, but the

nutrient values shown may have to be adjusted to a value for water determined individually. Several more or less alternative common names are given as well as the botanical names, but it seems likely that investigators may find difficulty at times in placing certain local foods. *H. E. Harding.*

Edison, Ann O., Silber, R. H. & Tennent, D. M. **The Effect of varied Thiamine Intake on the Growth of Rats in Tropical Environment.** *Amer. J. Physiol.* 1945, Oct. 1, v. 144, No. 5, 643–51, 3 figs. [14 refs.]

Comparable groups of rats were maintained under two environmental conditions: a "tropical" environment of 90°F. and 70 per cent. humidity, and a "temperate" one of 72°F. and 50 per cent. humidity. They were given a basal diet of casein, dextrose, hydrogenated vegetable oil, salt mixture and cod liver oil. Vitamins of the B group were either added to the diet or given separately in constant adequate amounts, except for thiamin, the quantity of which was varied from 300 to 2μ gm. daily.

When placed in a tropical environment, rats lost weight rapidly, but after a few days resumed growth at a stable but slower rate. Food consumption in tropical conditions decreased by 30–50 per cent.; the anorexia was not due to thiamin deficiency. The weight of these rats was 15–25 per cent. less than that of rats given a similar diet *ad libitum* in temperate conditions, but 15–25 per cent. greater than that of animals in the temperate environment whose diet was restricted to amounts exactly similar to those taken by the tropical animals.

When the thiamin intake of rats kept in each environment and previously given adequate amounts of thiamin, was reduced to 2μ gm. thiamin daily, the rate of loss of weight was less under tropical than under temperate conditions. There were indications also that polyneuritis developed more rapidly under temperate conditions.

Assays of the livers of these animals showed that the thiamin content varied with the dietary intake, but was unaffected by changes of environment.

The authors conclude that the thiamin requirements for the growth of rats in a tropical environment are not greater, and may be less, than in temperate conditions. *H. E. Harding.*

Bien, W. N. **Bisulphite Binding Substances in Human Blood.** *Chinese Med. J.* Washington. 1944, Oct.–Dec., v. 62, No. 4, 358–65. [15 refs.]

"The blood content of bisulphite binding substances was determined in various clinical conditions. The results are not conclusive enough to warrant the assumption that whenever the B.B.S. are elevated, beriberi is present. The present experience indicates that only when renal insufficiency, starvation and diabetic acidosis are not present, an elevation of the B.B.S. in the blood may indicate beriberi. Conversely, a lack of increase of B.B.S. in the blood does not rule out beriberi. The possible substances in the blood which combine with bisulphites are enumerated and briefly discussed."

Trowell, H. C. & Muwazi, E. M. K. **A Contribution to the Study of Malnutrition in Central Africa. A Syndrome of Malignant Malnutrition.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Dec., v. 39, No. 3, 229–43, 4 figs. on 3 pls. [38 refs.]

This paper appears to have been written earlier than one published by the same authors in *Arch. Dis. Childhood* (this *Bulletin*, 1946, v. 43, 143). It describes some features of a syndrome, common in Uganda, as observed in 200 patients at Kampala in 1943. The condition accounted for about 10 per cent.

of the medical admissions of adults, and about 50 per cent. of the children. Of the 144 adult cases, 25 were fatal, as were 10 of the cases in children.

Rough estimates are given of the diets of the natives amongst whom the condition occurs commonly. These show that the very poor labourer's diet is seriously deficient in everything except ascorbic acid; the immigrant labourer's diet is seriously deficient in calories, protein, calcium, vitamin A and nicotinic acid, and moderately deficient in iron and thiamin; the Ganda peasant diet on to which most of the children concerned were weaned when well into their second year, is moderately deficient in protein, calcium and nicotinic acid, and probably somewhat deficient in vitamin A, thiamin and riboflavin.

The soft brown hair and pallor of the facial skin, that are a common early sign in children, are often absent in adult cases. Children seldom show the crazy-pavement dermatosis of adults, and many of them have no looseness of the bowels. Most of the features of the syndrome, however, are present at all ages. The clinical picture consists of a gross loss of body weight in adults or a failure to grow in children, oedema, pallor of the skin and hair, crazy-pavement dermatosis, loose stools, steatorrhoea in children, macrocytic anaemia, slight mental and neurological changes, and a deficiency radiographic bowel pattern.

In the absence of sufficient details of the radiographic appearance of the normal African small intestine, the authors accept only segmentation, gross irregularity, coarseness or loss of the mucosal folds as evidence of abnormality. Of 23 adults examined, 19 showed frank segmentation, five had an abnormal mucosal pattern, and none was normal; 7 of the 9 children examined showed frank segmentation.

Undigested remnants of food were found in the faeces of about half the cases.

Mean figures and the range are given for blood counts on the 200 cases. The syndrome was usually accompanied by a macrocytic hypochromic anaemia, but at times the anaemia was normocytic, and not infrequently orthochromic. Examination of the sternal marrow in 101 cases showed a normoblastic erythropoiesis. Plasma proteins are given for 11 adults and 3 children. The mean plasma albumin was 2·05 gm. per 100 ml. with a range of 1·10 to 3·02: the mean plasma globulin was 4·05, ranging from 1·44 to 6·77. The albumin/globulin ratio was less than 1 in all but 2 cases.

Details are given of autopsies on two male adults.

On the ordinary hospital diet progress was slow in every respect. When thiamin was given in addition to the basic diet, definite improvement was reported by many of the patients, usually within 5 days. The improvement was largely subjective: no change was noted in the oedema. Giving nicotinic acid to patients taking the basic diet also led to an improvement in the condition of the majority, usually within a week. This consisted of a peeling of the dermatosis; no definite effect on the diarrhoea was observed. Injections of crude liver extract led to a reticulocytosis and a satisfactory increase of red cells and haemoglobin in almost all cases.

The syndrome appears to be distinct from pellagra and from nutritional oedema; it is very resistant to treatment by improvement of the diet or by supplements of the common vitamins, and it has a high mortality. It is proposed to call it "malignant malnutrition." *H. E. Harding.*

GILLMAN, J. & GILLMAN, T. **Structure of the Liver in Pellagra.** *Arch. Pathology.* 1945, Oct., v. 40, No. 4, 239–63, 22 figs. [Refs. in footnotes.]

This long but interesting paper gives first a detailed account of the histology of sections of livers obtained by biopsy from 120 pellagrins on the day of their

admission to hospital. The livers are divided into four groups, each with further subdivisions that depend upon the quantity of fat present. In the first group the livers show varying amounts of fat only ; livers in the second group show cytosiderin (haemosiderin) and cytolipochrome (haemofuscin) in discrete granules in hepatic and Kupffer cells : the third group is similar to the second but iron-containing pigment is found also aggregated in large masses in cells lying either in the hepatic lobule or in portal tracts : the last group shows pigment cirrhosis. Fatty livers of the first group are the invariable finding in infants suffering from pellagra ; no disturbance of iron metabolism is found at this age. Pigmented livers with or without visible fat are found in adolescents and adults.

Evidence is given that pigment is formed in the cells at a time which coincides with the disappearance of fat. The amount of pigment formed varies from case to case, the extent and the intensity of pigmentation giving an excellent indication of the degree of chronicity of the disease. The iron pigment arises within the liver cells as a result of a profound disturbance of intracellular metabolism induced by dietary imbalance. Both pigments appear to originate from mitochondria. Exacerbations of the acute stage may lead to reappearance of fat in livers which already show pigmentation from previous damage.

Repeated attacks of pellagra may cause a fatty condition to progress to frank pigmentary cirrhosis. Such cirrhosis was found in an eighth of all the pellagrins examined, or in 15 per cent. of the adults. There was strong presumptive evidence that the incidence of cirrhosis might be as much as 30 per cent. Pigment cirrhosis occurred mainly under the age of 40 years, and was indistinguishable clinically and pathologically from haemochromatosis. Evidence is given for the view that this condition is not a result of an inborn error of metabolism, but is one of the manifestations of chronic malnutrition.

The authors believe that therapy and the assessment of its effectiveness in pellagra should be based not only on the clinical picture, but more especially on the structural alteration in the liver in each case. They suggest that, in pellagrins, fatty change, formation of intracellular pigment with or without cirrhosis, and hepatic carcinoma represent different patterns of reactivity of liver cells to acute and chronic malnutrition. *H. E. Harding.*

GILLMAN, J., GILLMAN, T. & BRENNER, S. **Vitamin A and Porphyrin-like Fluorescence in the Livers of Pellagrins, with special reference to the Effects of a High Carbohydrate Diet and Methionine.** *South African J. Med. Sci.* 1945, Sept., v. 10, No. 3, 67–86, 4 figs. [36 refs.]

Fragments of liver obtained by biopsy from 60 adult and infant pellagrins were examined by fluorescence microscopy for the presence of vitamin A. There appeared to be a reciprocal relationship between the amount of fat in the liver cells and the amount of vitamin A fluorescence in the Kupffer cells : there was very little fluorescence in very fatty livers. In rather more than half the cases examined the amount of fluorescence was well below the average normal. The effects of a diet free from vitamin A, but containing a high proportion of carbohydrate, were erratic ; the amounts of vitamin A fluorescence varied in an unpredictable manner. Administration of large quantities of vitamin A in conjunction with a full diet, appeared to aggravate the disease, and did not lead to as great an increase in vitamin A fluorescence as did ventriculin with a similar full diet. The fatty livers of two pellagrous children did not respond to methionine, and there was afterwards a delay in the response to ventriculin.

Phrynoderma was observed in two patients whose livers showed marked vitamin A fluorescence : three patients, whose livers showed no fluorescence, had no evidence of phrynoderma. It is concluded that phrynoderma cannot be regarded as due to vitamin A deficiency.

A porphyrin-like fluorescence was seen in the liver cells of a few pellagrins. [More details of this are given in the following paper.] *H. E. Harding.*

GILLMAN, J., GILLMAN, T. & BRENNER, S. **Porphyrin Fluorescence in the Livers of Pellagrins in relation to Ultra-Violet Light.** [Correspondence.] *Nature.* 1945, Dec. 8, 689.

The examination, by ultra-violet fluorescence microscopy, of frozen sections of fragments of livers removed by biopsy from 20 African pellagrins, soon after admission to hospital, showed the presence of an intense scarlet-red fluorescence in eight cases. Reasons are given for believing that this fluorescence was due to a porphyrin. Patients kept on a carbohydrate diet poor in vitamins lost this fluorescence in their livers : exposure of the patients to ultra-violet light then led to a recrudescence of the fluorescence, but not to aggravation of the skin lesions. Traces of porphyrins were found in the urine of only one patient.

The authors conclude that : (1) Porphyrin fluorescence in the liver can occur during the acute phases of pellagra. (2) The great accumulation of iron pigment in many livers of adult African pellagrins is probably caused by the disruption of an intracellular iron porphyrin complex, such as catalase and cytochrome, present normally in the liver cell. (3) Treatment with vitamin B complex is not required to resolve the porphyrin fluorescence in the livers of pellagrins while on a carbohydrate, vitamin-poor, diet. (4) Ultra-violet light can excite a recrudescence of the porphyrin fluorescence in the liver without causing an exacerbation of the other external manifestations of the disease. Massive quantities of porphyrins can appear in the liver cells without any detectable amounts in the urine. (5) These experiments emphasize the close inter-relationship between the reactivity of the skin to ultra-violet light and the deposition of iron and the appearance of porphyrin fluorescence in the liver of African pellagrins. *H. E. Harding.*

SPRUE.

LEISHMAN, A. W. D. **Thoughts on Sprue after Experience in India.** *Lancet.* 1945, Dec. 22, 813–15. [17 refs.]

From 1942 to 1945 the incidence of sprue amongst troops in India and the South-East Asia Command has been particularly heavy ; in 1944 alone 675 patients were invalided on account of this disease. The diagnosis of this syndrome presented few difficulties when it was recognized that dysentery alone was not the sole cause of diarrhoea in the tropics. On the therapeutic side there remains considerable need for improvement, and " even the most specific remedy, liver extract, acts in a manner quite unknown." Though in India there appears to be reluctance in recognizing sprue in Indians, nevertheless this attitude does not appear to be wholly justifiable. What has been termed the marasmic syndrome, when coincident factors of malaria, dysentery, ankylostomiasis and malnutrition have been eliminated, appears to be indistinguishable from sprue. A somewhat novel observation is that three-quarters of the [European] patients had less than 2 years' tropical service when they first developed the disease ; that length of residence is scarcely a factor, as has been previously assumed, was illustrated in one patient, who disembarked

from his ship in Bombay with fully-developed sprue, after having spent 2–3 weeks in Durban on his way from Britain. In war-time sprue observed a distinct seasonal incidence, from March to September, with a peak incidence in June, during the months corresponding to the fly season (with consequent dysentery), and to the malaria transmission season.

Sixty-five per cent. of cases originated in Bengal, Assam and Burma, but 15 per cent. came from Western India, 13 per cent. from South India and Ceylon, and 5 per cent. from North India; one-third were soldiers living on full rations and usually in an entirely innocuous climate.

In view of the work of HOWAT, which indicated that the use of sulphaguanidine in bacillary dysentery provokes steatorrhoea, it is striking that a history of frank dysentery was obtained in only 9 per cent. of cases; of these 4 per cent. were amoebic, 3·5 per cent. bacillary, and the rest "clinical".

In more than half of the patients, the syndrome was fully established within two months of the onset of diarrhoea, but in 20 per cent. the interval was as short as 3 weeks. Loss of weight was an outstanding feature, and in 95 per cent. it was not less than 20 lb. Almost all the patients had changes affecting the mouth, lips or tongue; 20 per cent. had skin changes—follicular hyperkeratosis (a sign of vitamin A deficiency) and parakeratosis (probably a vitamin B deficiency). Well-marked pigmentation, especially of the face, was occasionally seen, but never the skin changes of pellagra.

Dark-adaptation tests and slit-lamp examinations of the cornea showed no significant abnormalities in patients so tested.

Dyspepsia.—Flatulent dyspepsia was invariably present, increasing towards the latter part of the day; a common symptom was retrosternal burning pain.

Stools.—One important fact emerges. In 20 per cent. of cases there was no apparent increase of fat in the stools. A possible explanation is that owing to the increased bulk of the faeces due to débris and bacteria, a sample estimation does not give a true picture of fat excretion. A second anomaly concerned the pigment in the stools, the presence or absence of which affords no real indication of the fat content, for stools of normal colour have been found to contain great excess of fat, and *vice versa.*

Leishman reverts to a formerly widely held hypothesis that the normal stool pigment in sprue is reduced to a colourless compound and that this constitutes a classical feature of the syndrome. [A reduction product of hydrobilirubin in sprue was described by NENCKI and an account of its chemistry is given by VAN DER SCHEER in Mense's *Handb. der Tropenk.*, 1905, v. 1, 20. This was investigated by the reviewer in Ceylon. A colourless extract was obtained by trituration of the freshly-passed faeces in 90 per cent. alcohol, and filtration. When exposed to the sunlight or shaken with air the extract changed to light yellow or brown. The same effect was produced by the addition of a drop of nitric acid. There appeared to be grounds for supposing that hydrobilirubin is present in sprue faeces, but that the greater part is reduced to leucourobilin. That normally coloured bile is secreted in sprue has been ascertained at post-mortem. According to STRASBURGER, "*Die Fäzes des Menschen*" 1910, leucourobilin is identical with urobilinogen. See also a Report on Researches in Sprue in Ceylon 1912–1914, Cambridge University Press, pp. 50–51.]

More than half the cases had acid curves (by test-meal) within normal limits.

The author satisfied himself that full recovery from sprue could be made in India, and he supports the opinion that when once a patient has fully recovered a return to India may be permitted. There were seven fatal cases, a case-mortality rate of about 1 per cent. The cases which give rise to anxiety are those which are profoundly emaciated, with a striking degree of hypotension,

although there is some dehydration, hydration achieves only limited improvement and desoxycorticosterone is without effect. In cases of this type there is consistently a diminished plasma-volume with low blood sodium and chloride, the potassium level being normal. Plasma proteins were slightly diminished but not to the extent found in starvation cases. In the few cases in which hypochloraemia, as well as the dehydration, was treated, the response was not striking; plasma transfusion had little advantage over saline. It seemed clear that no form of parenteral therapy could act as a substitute for food given by the mouth.

As regards aetiology, the author considers that in many respects sprue behaves like an infection; although usually sporadic it occasionally attains epidemic proportions. In 1943 in Chittagong nine separate units were affected and in some the incidence was 50 per cent. In one R.A.F. unit, within 3 weeks of arrival there, 10 per cent. of the men had diarrhoea which rapidly developed into sprue. It was thought at the time that some tinned meat might have been a factor in causing the initial enteritis. The popular idea of "sprue houses" would suggest some infective agent, but none has yet been found.

The author agrees with STANNUS (1942) that interference with the absorptive process is the result of failure in the phosphorylation of fatty acids. The primary failure in sprue is lack of vitamins of the B group (well-known and [perhaps] unknown), for, without these, phosphorylating enzymes cannot be constituted. By accepting this view, however, difficulties are encountered, for in sprue a history of inadequate vitamin-intake is seldom obtained. The whole concept of vitamin B deficiencies may need to be recast in the light of recent knowledge of biosyntheses by intestinal bacteria. BENESCH [*Bulletin of Hygiene*, 1945, v. 20, 564] provided evidence that nicotinic acid is synthesized by aerobic, and destroyed by anaerobic, organisms within the human intestine, and that in health an equilibrium must exist between those which produce and those that destroy vitamins. The "infective character" of sprue may now become capable of a more liberal interpretation, and be linked with the conception of sprue as a deficiency disease; synthesizing organisms may be swamped by infection with non-synthesizing organisms which otherwise are not pathogenic, and stagnation in the small intestine due to unaccustomed diet may provide a medium in which the latter flourish.

This hypothesis has the merit that it can be put to the test. A series of vitamin-excretion estimations in patients with sprue and in controls on a standard low vitamin diet should be made, together with an investigation of the small intestine flora on the lines employed by BENESCH, to determine the relative proportions of aerobes and anaerobes and their ability to synthesize nicotinic acid and other members of the B group. For this purpose samples must be collected by means of the Miller-Abbott tube, which, it has been found, can be used in sprue. *Philip Manson-Bahr.*

KEELE, K. D. & BOUND, J. P. **Sprue in India. A Clinical Survey of 600 Cases.** *Brit. Med. J.* 1946, Jan. 19, 77–81, 2 figs.

For the present purpose sprue is defined as a syndrome, consisting of diarrhoea, with the passage of light-coloured stools of high fat content, sore tongue, flatulent dyspepsia, and emaciation. Malnutrition may indeed manifest itself as the sprue syndrome, but steatorrhoea is too variable a feature upon which to separate the two, and the syndrome, as defined above, has been diagnosed as sprue, "even in the presence of an isolated normal faecal fat."

Throughout India during the recent war period the incidence of sprue was highest in May and June; it was minimal in November, December and January, in both 1943 and 1944. This applied whether the cases originated in the cool climate of the Assam Hills (54 per cent.) or in the hot plains of Bengal

and Bihar (23 per cent.) or in the rest of India (23 per cent.). The geographical distribution of 450 cases was: Assam and N. Burma, 54·2 per cent.; Bengal and Bihar, 23·1 per cent.; S. India and Ceylon, 9·1 per cent.; Bombay Presidency, 8·9 per cent.; N.W. and Central India, 4·7 per cent.

Within a climatic zone sprue is regional. For instance, 14 per cent. of cases in the present series occurred near Imphal, and the high incidence in this place continued long after the siege had been raised. Chittagong (9 per cent.) on the coast, at the edge of the Ganges delta, produced quite a nest of cases—six from one aerodrome in two weeks. The difference in climate between these two localities illustrates how the local regional factor may supersede that of climate. The maximal incidence occurred after one or two years' service in India. The earliest was in the Red Sea *en route* to India. Heat adaptation was probably not an important factor.

In a comparison of the seasonal incidence of sprue and dysentery (amoebic and bacillary), it was found that the incidence of sprue precedes that of dysentery, suggesting that it is unlikely that sprue commonly follows an attack of dysentery. In 23·6 per cent. of cases dysentery preceded sprue, but there was no significant difference between the incidence of dysentery in the cases of sprue. In some individual cases, however, a close relationship is found to exist between an attack of amoebic or bacillary dysentery and the sudden passage of sprue stools; the effect of the dysentery may be non-specific in activating the latent syndrome. In one group of 87 cases labelled "malnutrition" in the Chindit Forces (in June and July 1944) were included 52 with the sprue syndrome. Analysis of the stools of 15 showed 12 with faecal fat over 30 per cent. Malaria was frequent and whilst response to sprue therapy was unsatisfactory, improvement was dramatic after the development and subsequent treatment of malaria. Although the brunt of incidence of sprue falls on Anglo-Indians and Europeans, it is undoubtedly true that Indian troops have developed the full syndrome during this war.

Regarding the influence of diet little information of value was forthcoming. Most of the patients developed diarrhoea under jungle conditions, but many were on field service rations. A large number became ill on a diet composed of protein 95–103 gm.; fat 114–143 gm.; carbohydrate 425–435 gm.; with calcium 1·6–1·7 gm.; iron 20–25 mgm.; vitamin A 1450 I.U.; thiamin 1·2–1·8 mgm.; riboflavin 2·1 mgm.; niacin 16·3 mgm.; ascorbic acid 6 mgm. (with supplementary tablets of 50 mgm.). This diet, well-balanced and adequate as it appeared, was found monotonous and distasteful.

In contrast to the classical picture the type of medical history was as follows:—After jungle training and contracting the customary short fevers and dysentery, the soldier became involved in fighting in Burma, and subsisted on the diet already detailed. The onset of diarrhoea was gradual and was usually attributed by the patient to his diet. Soon anorexia and glossitis were noted, with flatulent dyspepsia and heartburn. After reporting sick he was admitted to hospital and rapidly improved, but on returning to duty the diarrhoea recommenced and the typical sprue syndrome evolved. The result might be mild acute sprue with continual relapses if, as so often happened, he was returned to duty in India. The severe form proceeds from the onset to produce dehydration, emaciation and a smooth dry tongue. Steatorrhoea is obvious; severe anaemia may develop suddenly, necessitating transfusion. Though response to treatment is often satisfactory, men with this type had to be evacuated from India. On an average the period between onset and evacuation was about one year, in both mild and severe cases.

Post-dysenteric sprue was noted especially after amoebic dysentery; in these cases the sprue syndrome was either temporary, or severe and long-standing.

Several instances of subacute hepatic necrosis, without jaundice, were observed in which there were symptoms of sprue ; the latter improved as the liver diminished in size.

The clinical picture of " incomplete sprue " was seen in 3·6 per cent. of cases ; the diagnosis noted on the finding of steatorrhoea and other signs of sprue in cases of chronic diarrhoea which had been treated as chronic dysentery. At the other extreme are cases of glossitis with minimal steatorrhoea conveniently termed " larval sprue." In this series 20 per cent. had total faecal fat of less than 30 per cent. and it is more than probable that the numbers with normal fat excretion would have been greatly reduced had it been possible to repeat the examination.

Glossitis was practically constant (96 per cent.) in this series and the longer the cases were observed the fewer were the exceptions. The tongue changes were found very variable, but coincided within a day or two, with diarrhoea. Glossitis responded surprisingly quickly to diet, but administration of nicotinic acid and riboflavin often seemed to accelerate improvement. Cheilitis and angular stomatitis occurred in 40 per cent. and did not respond so quickly. The typical magenta tongue of riboflavin deficiency was not seen. The appetite ranged from extreme voracity to extreme anorexia. Rash increase of diet, on the return of appetite, provoked relapse. Vomiting was present in 18 per cent. particularly in cases of acute onset. Heartburn was common, and caused considerable distress ; dysphagia was not marked. Dyspepsia, on the other hand, of the flatulent type was practically constant (94 per cent.), and was exacerbated by administration of fats ; the gastric juice, however, was normal in at least 66 per cent. Distension, a salient feature, appeared early and disappeared late, being maximal in the hypogastrium. The abdominal girth altered by 1–2 in. only, though the patient's sensation leads him to expect more. Barium meal examinations failed to show convincing evidence of small intestine dilatation, but one instance of megacolon was found in one who did not exhibit undue distension, but made a good recovery. Diarrhoea often as acute and as painful as in dysentery, with passage of 15–20 pale, watery stools, was a constant feature, and its response to sulphaguanidine was similar to that of dysentery, but the stools were devoid of exudate, and there was neither pyrexia nor leucocytosis. The onset of sprue was often sudden and unexpected. Diarrhoea preceded glossitis by about six weeks in 80 per cent. of the cases ; the reverse very rarely.

On admission most patients had lost 25 per cent. of their normal Indian war-time body weight. The average loss ranged from 20 to 60 lb. at body weights of 130 to 195 lb.

Cramps, usually in calves and thighs, were present in 25 per cent. No osteoporosis was observed. Chvostek's and Trousseau's signs were negative except in one solitary case. Response to liver, nicotinic acid, calcium gluconate, salines and transfusions was satisfactory from the clinical viewpoint.

Dry skin with depilation was common, whilst scaling of parakeratotic type occurred in 27 per cent. Follicular hyperkeratosis responded quickly to treatment and cleanliness and, though it suggested a vitamin A deficiency, dark adaptation tests were normal in 19 of 20 patients with one exception. Pigmentation occurred in 4 per cent. and was so extensive in one patient as to suggest haemochromatosis. The distribution did not suggest pellagra.

Hypotension below 100/70 was noted only in 8 per cent., all severe cases with dehydration and low urinary chlorides ; this hypotension persists and rises slowly in response to treatment. No evidence of left- or right-sided heart failure was found.

It was thought that these cases would present examples of typical deficiency states, but this did not turn out to be so. In some obdurate cases of glossitis

nicotinic acid proved effective, but though glossitis with angular stomatitis was common, other signs of riboflavin deficiency were absent. No case showing evidence of vitamin B_1 or C deficiency was seen.

Pallor of the faeces at some period was almost constant, and was due not only to the high fat content, but also to alteration of bile pigment. A pale stool may have a normal fat content, a coloured stool may have a raised fat content. Microscopically, fatty acid crystals, fat globules and soaps may be seen, but give little guide to quantitative fat excretion. Analysis of single stools showed great variability; two consecutive specimens, for instance, showed 21 per cent. and 36 per cent. total fat content, respectively. For routine examination, 24-hour collection of stools, well mixed, should be a minimum procedure. A further proviso is that the daily fat intake for at least the three previous days should be known. In 10 normal persons, the total fat averaged 30 per cent. on a fat intake of 70 gm. daily, but in 20 per cent. of the cases of sprue the faecal fat was below 30 per cent.; conversely high faecal fat above 50 per cent. did not indicate clinical severity. Fat-splitting was excessive; in the majority of 274 cases the ratio of split to unsplit fat was between 3–1 and 10–1. The high ratio might be interpreted as due either to delayed absorption or to excessive lipase action. Hyperchlorhydria or normal acid curves were present in 66 per cent.; in 27 per cent. hypochlorhydria (less than 10 units HCl) was present.

Severe anaemia was uncommon even in clinically severe cases, though "blood crises" were observed in a few. The few blood-sugar curves which were carried out showed normal fasting values with the low rise, as generally described in sprue.

The object of treatment was to make the patients fit to travel, and the authors have not made innovations; they do, however, remark on the value of parenteral crude liver extract in severe cases. The response to sulphaguanidine in acute cases up to a total of 70 gm., was found to be good. Immediate prognosis for life was good. No patient in the 600 of this series died. Of 40 cases followed up for one year six have had severe relapses and the remainder less severe recurrence of symptoms; none has remained quite well.

Philip Manson-Bahr.

HAEMATOLOGY.

EVANS, R. W. **Anaemia associated with the Sickle Cell Trait in British West African Natives.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Dec., v. 39, No. 3, 207–20. [12 refs.]

A diagnosis of sickle cell anaemia based solely on the association of anaemia with sicklaemia is unjustified, as factors other than sickling of the cells may be responsible for the anaemia of patients with the sickle cell trait. In one series of patients suffering from anaemia associated with sicklaemia, the sickle cell haemolytic crises may well have been initiated by anaemias of different aetiology. Complete haematological investigations showed such underlying conditions as megaloblastic nutritional anaemia, hypoplastic anaemia of undetermined origin, and anaemia due to hookworm infection, dietary deficiency and malaria. In unmasking the bases of these anaemias the value of bone marrow examinations has been shown repeatedly. During a sickle cell crisis the marrow shows an intense erythroblastic and leucoblastic hyperplasia with considerable increase in the number of monocytes, many of which may contain engulfed red cells. The normoblasts tend to be large, early eosinophilic forms

with a well patterned nucleus, such as are found in haemolytic anaemias and in conditions of prolonged loss of peripheral blood. The diagnosis of a sickle cell haemolytic crisis will therefore be suggested by an anaemia with leucocytosis, jaundice and a hyperplastic bone marrow which shows no abnormal cells, occurring in a patient whose red cells have been shown to exhibit sickling *in vitro*. It is then confirmed by the demonstration of sickle cells *in vivo*.

In a second series of patients the sickle cell crises appeared to have been precipitated by other more urgent diseases or acute toxic conditions, such as tropical myositis and blackwater fever, meningitis, and Addison's suprarenal disease. In these the spleen at autopsy presented as a small, hard, nodular grey organ. Cut sections showed thickened trabeculae and yellowish-brown nodules scattered throughout the pulp—the result of organization of haemorrhagic areas. The pulp itself had been transformed into a reticular mass packed with sickle cells. These extensive, degenerative changes may be taken as evidence of frequent sickle cell crises that had occurred in the past. Lesions found in other organs are fundamentally similar to those which have been described in the spleen, namely, tissue destruction by haemorrhage and thrombosis followed by necrosis. These observations suggest that the chief feature of the condition is not the anaemia but the liability to thrombosis which occurs during a sickle cell crisis. The term " sickle cell disease " would therefore appear to be preferable to " sickle cell anaemia ". *F. Murgatroyd.*

Altmann, A. **The Sickle-Cell Trait in the South African Bantu.** *South African Med. J.* 1945, Dec. 8, v. 19, No. 23, 457. [20 refs.]

" Of 403 blood specimens of South African Bantus, only one showed the sickle-cell trait in a moist sealed preparation after 24 hours' incubation at 37°C. The sickle-cell trait, which is very common in the West African and American negro, is rare in the South African Bantu."

Woofter, A. C., Dick, W. S. & Bierring, W. L. **Sickle Cell Anemia in White Patients with Ulcers of the Ankles. Report of Two Cases.** *Arch. Intern. Med.* 1945, Oct., v. 76, No. 4, 230–33, 4 figs. [Refs. in footnotes.]

Sickle cell anaemia is almost exclusively a disease of the Negro race, although several instances of the disease have been reported in patients thought to be without Negro ancestors. Ulcers on the legs or ankles, unilateral or bilateral, have appeared spontaneously or after mild trauma in Negro patients suffering from this condition ; healing is prolonged and followed by scarring. Hitherto, however, all available case histories of the disease in the white race have failed to mention or have noted the absence of ulcerations or scars about the ankle joints.

The present report describes two patients, from one family, suffering from sickle cell anaemia, with ulcers of the ankles and limitation of motion about the ankle joints. The first patient, a 20-year-old white youth, was admitted to hospital complaining of ulcers on both ankles, the ulcers having appeared when he was 13 years of age, after an attack of dermatitis venenata (ivy poisoning), and having persisted until the time of his admission to hospital. The second patient, the 14-year-old sister of the first, had a small ulcer on the right ankle, which had existed for approximately three weeks. Both patients were anaemic, and 15 and 18 per cent., respectively, of their erythrocytes showed sickling. Other physical and laboratory findings were confirmatory of sickle cell anaemia ; the Wassermann and Kahn reactions were negative. The family history revealed that the paternal grandmother had been pale and suffered from ulcers of the ankles, and that the father and an uncle had both been pale and had had scarring and fixation of both ankle joints. The parents

of the grandmother, the first reported member of the family with the disease, were known by a local historian to have been normal and of the white race. [The remainder of the ancestry is not recorded; it may have contained a negroid element.] *F. Murgatroyd.*

TOMLINSON, W. J. **A Study of the Circulation of the Spleen in Sicklemia and Sickle Cell Anemia.** *Amer. J. Path.* 1945, Sept., v. 21, No. 5, 877–87, 6 figs. on 3 pls. [12 refs.]

Histological changes in the spleen in sicklaemia have been stated to be congenital in origin, but in a large number of cases no congenital vascular abnormalities have been found. It is possible, therefore, that the splenic picture may result from the sickle cells.

In the normal spleen, follicular capillaries arise from the central arteries, pass through the substance of the follicles and terminate just beyond the marginal zone by numerous small openings into the red pulp, always at considerable distances from the nearest venous sinuses. Follicular capillaries frequently unite by short branches. In some instances the endings are distended, presenting ampullae, with restriction of erythrocytes but permitting the escape of plasma through the endothelial walls; in others, large openings between the endothelial cells allow the passage of erythrocytes into the pulp cords, and thence through stomata into the venous sinuses. Capillaries of the marginal zone arise from branches of the follicular capillaries passing into the red pulp, where they branch, the small branches terminating in the marginal zone of the follicle in the pulp spaces; the tips of these capillaries are usually distended into thin-walled ampullae with narrow clefts leading into the pulp spaces. Capillaries of the pulp cords are branches of the capillaries of the marginal zone and terminate in the pulp spaces, with or without ampullae, and in some cases perhaps open directly into the venous sinuses. It seems however, that the circulation of blood in the spleen is open, with the pulp spaces constituting the connexions between the arterial and venous channels.

Routine autopsy sections of spleen from 150 cases of sicklaemia and 24 cases of sickle cell anaemia showed no evidence of congenital or other abnormalities of the arteries or arterial capillaries. In most cases " pooling " in the marginal zone was marked. The sickled erythrocytes were compressed and packed, usually in a circular, lamellated fashion with obvious overlapping, in the dilated pulp spaces. The venous sinuses were generally collapsed.

In preparations perfused through the arteries, the erythrocytes were washed out of the arteries, arterial capillaries, and the venous sinuses, but were present in the pulp cords, especially in the marginal zones, which obviously represented the " pools ". There was no evidence of abnormal dilatation, congenital defects, or of direct emptying into the venous sinuses. It is impossible, therefore to explain the " pooling " in the marginal zones by changes in these arterial capillaries.

Venous perfusion produced filling of the small venous sinuses with erythrocytes, and emptying of the arterial channels. The pulp cords contained erythrocytes and the " pools " were accounted for by these distended pulp cords; no evidence of reverse flow of erythrocytes from the pulp cords into the arterial capillaries was present. It appeared that the perfused fluid carried the erythrocytes from the larger veins back into the smaller venous sinuses; then the fluid escaped from the venous sinuses into the pulp spaces through the stomata, and then into the arterial capillary endings in the pulp cords, washing out the erythrocytes originally present in these capillaries. No abnormalities were demonstrated in the arterial capillary terminations or ampullae, and no " pools " were produced in the venous sinuses, despite the reversal of the circulation.

No vascular abnormalities were found in sections of spleens perfused with distilled water until the water was clear, the organ then being fixed in the distended state ; and it was impossible to distinguish the sections of sicklaemia cases from normal spleens similarly treated. Sections digested in pancreatin and stained for reticulum also showed no clear abnormalities.

The histological picture in sickle cell anaemia resembles that of chronic hyperaemia, with the pulp cords, especially in the marginal zones, packed with lamellated sickle cells that do not, because of their shapes, readily escape through the stomata. In sickle cell anaemia there are always some sickled cells present *in vivo*, and although the degree of sickling is variable, there will be constantly " pooling " and packing of these sickled forms, resulting, in time, in thrombosis, haemorrhage, deposition of calcium and iron, and leading eventually to the formation of the small fibrotic spleens found in older, active cases of sickle cell anaemia. *F. Murgatroyd.*

SCHIEBER, C. **Target-Cell Anaemia : Two Cases in Bucharan Jews.** *Lancet.* 1945, Dec. 29, 851–2, 2 figs. [12 refs.]

Target-cell anaemia, a familial haemopoietic disorder of adults, is characterized by the presence in the peripheral blood of large abnormal red cells which look like targets. The anaemia is hypochromic and haemolytic, although the red cells show an increased resistance to hypotonic saline solutions ; the bone marrow is hyperplastic ; and there are usually skeletal changes, including mongoloid facies and thinning of the cortex of long bones, with well-marked trabeculation, radiologically resembling that found in Cooley's anaemia. Cooley's anaemia, restricted to people from the Eastern Mediterranean littoral and regarded, until recently, as invariably fatal, is an erythroblastic anaemia of children ; the suggestion is now made that target-cell anaemia is an anerythroblastic adult form of Cooley's anaemia.

After splenectomy in target-cell anaemia, an increase in the total red cell count, and in the ratio of target-cells to normal red cells, suggests that destruction of target-cells in the spleen is responsible for the haemolytic character of the disease, since splenectomy in other haemolytic anaemias never leads to the appearance of target-cells in the circulating blood. A further suggestion that hyperbilirubinaemia might lead to the presence of target-cells cannot be substantiated, firstly because these cells have been found in healthy members of affected families in whom no excess of bilirubin was present, and secondly because the hyperbilirubinaemia of other haemolytic anaemias is not associated with the formation of such cells.

The author describes two cases of target-cell anaemia in one family of Bucharan Jews. The first patient was a 14-year-old girl suffering from a fatal subacute bacterial endocarditis. As some of the clinical features could not entirely be fitted into the diagnosis of endocarditis, it was thought that she had some unrecognized familial blood dyscrasia, and it was decided to investigate her brother in greater detail. In her blood there were many target-like erythrocytes, a similar condition being found in her brother ; no sickle cells were found. She had a mongoloid facies and a history of pallor for many years ; both these features were present in the brother, the rest of the family being healthy. There were round pigmented scars of indolent ulcers on both her shins. Her blood showed an increased resistance to haemolysis by hypotonic saline solutions.

The second patient, her brother aged 30 years, had a mongoloid facies with a wrinkled yellowish skin, an appearance said to have been present since he was aged 9 years. He seemed to have been anaemic for many years, and although never febrile, and although parasites had never been found, he had,

like his sister, frequently been given quinine for supposed malaria. He was afebrile and not obviously ill, but full examination revealed further interesting features, which remained unaltered during the 2 years in which he was under observation. He had an enlarged heart with an apical murmur, a hard spleen reaching as low as the umbilicus, and loss of vision in the left eye, due to thrombosis of the left central retinal vein. Blood examination showed the following :—R.B.C. 3,000,000 per cmm. ; Hb. 7·5 gm. per 100 cc. ; haematocrit 25 per cent. ; M.C.V. 83 cμ. ; M.C.Hb. 25 $\mu\mu$gm. ; M.C.Hb. conc. 30 per cent. ; W.B.C. 6,000 per cmm., with a normal differential count. Films showed severe anisocytosis, poikilocytosis, and target-cells. The serum bilirubin was 2 mgm. per 100 cc. (indirect), and there was increased urobilinogenuria. The reticulocytes were 5 per cent. ; the bone marrow hyperplastic, with nucleated red cells forming 70 per cent. of the total nucleated cells. The erythrocyte resistence to hypotonic saline solutions was equivalent to 0·46–0·18 per cent. saline solution. The B.S.R. was 1 mm./hr. (Westergren). The serum calcium was 11·4 mgm. per 100 cc. ; serum phosphatase 0·8 Bodansky units ; serum proteins, total 7·62 gm. per 100 cc. ; serum albumin 5·06 gm. per 100 cc. Radiography of the bones showed thinning of the cortex to such a degree that many parts, especially metaphyses of long bones, looked like cysts, with only trabeculae crossing them ; there were no spontaneous fractures.

The author suggests that in target-cell anaemia, in addition to the hereditary defect in erythropoiesis, there may be a second, external, factor involved when haemolysis becomes manifest. In support of this hypothesis he states that among the Jewish population with which he worked, haemolysis is more likely to follow administration of sulphonamides in the dark-skinned Mediterranean than in the lighter-skinned immigrant Jew. *F. Murgatroyd.*

Spies, T. D., Vilter, C. F., Koch, Mary B. & Caldwell, Margaret H. **Observations of the Anti-Anemic Properties of Synthetic Folic Acid.** *Southern Med. J.* 1945, Nov., v. 38, No. 11, 707–9.

Non-specific reticulocytosis, not followed by a characteristic rise in haemoglobin and red cells, may occur after the administration of various substances. In the treatment of macrocytic anaemia, niacin, thiamin, riboflavin, calcium pantothenate, pyridoxine, inositol, paraminobenzoic acid, choline, pyridoxamine, pyridoxal, and crude folic acid concentrates were of little or no efficacy ; ascorbic acid caused reticulocytosis and sometimes blood regeneration in selected cases. The reticulocytosis, increase in erythrocyte count and haemoglobin level, and clinical upsurge of well-being, following the intravenous or oral administration of synthetic folic acid, *Lactobacillus casei* factor, were, however, sufficiently promising to warrant further studies of its effect on the regeneration of haemoglobin and erythrocytes. The substance, considered a part of the B complex, is described as active for *L. casei*, *S. faecalis* R, and as promoting growth and haemoglobin formation in the chick. *F. Murgatroyd.*

Vilter, C. F., Spies, T. D. & Koch, Mary B. **Further Studies on Folic Acid in the Treatment of Macrocytic Anemia.** *Southern Med. J.* 1945, Dec., v. 38, No. 12, 781–5.

Fourteen patients suffering from macrocytic anaemias, of which six were considered to be nutritional macrocytic anaemias, five Addisonian pernicious anaemias, and three of indeterminate type, were treated with synthetic folic acid, *L. casei* factor, and were observed for periods of one week to nine years, all but two being observed for more than six months. The folic acid was given in a variety of doses, intravenously, intramuscularly and orally. The dose, ranging by injection from 10 to 100 mgm. and averaging 20 mgm., was repeated

daily for two to three weeks for the most part, although reticulocytosis was observed after even a single dose ; by mouth, larger doses of about 100 mgm. were given daily for 19 to 38 days. Diets were regulated carefully so that the source of extrinsic factor would be minimal.

Thirteen of the patients showed a positive haematological response, consisting of reticulocytosis and subsequent rise of erythrocytes, haemoglobin and leucocytes ; and in cases where treatment was continued the regeneration progressed to normal levels, the responses to treatment paralleling those afforded by potent liver extract. In addition, a feeling of subjective improvement occurred between the third and fifth days of treatment, before the day of the initial reticulocyte response ; the symptoms were also improved, diarrhoea disappeared, glossitis cleared, while the paraesthesiae of " combined system disease " were partially relieved. Further studies have shown that synthetic folic acid is effective in treatment of the macrocytic anaemia of sprue, pellagra, and pregnancy ; it had no effect on anaemia due to iron deficiency, on several types of anaemia associated with hypoplastic bone marrow, and on " myelophthisic " anaemia due to aleukaemic myelogenous leukaemia.

F. Murgatroyd.

Paseyro, P. Contribución de la citologia en el diagnóstico de las afecciones de la sangre y de los órganos hematopoyéticos. [**Cytology in Diseases of the Blood and Blood-Forming Organs.**] *An. Facul. de Med. de Montevideo.* 1945, v. 30, Nos. 9, 10 & 11, 612–848, 142 figs. (1 coloured). [Bibliography.]

VENOMS AND ANTIVENENES.

Finlayson, M. H. & Hollow, K. **The Treatment of Spider-Bite in South Africa by Specific Antisera.** *South African Med. J.* 1945, Nov. 24, v. 19, No. 22, 431–3.

The chief cause of venomous spider-bite, " knopie " bite, in South Africa is the *Latrodectus*, either *L. indistinctus* or *L. geometricus*. Antivenenes against the former, prepared from goats, have been found effective in bites by the latter also. R. H. N. Smithers thinks that *L. indistinctus* is a colour variety of *L. tredecimguttatus* (of Southern Europe) and both *L. indistinctus* and *L. mactans* may be but variants of *L. tredecimguttatus*.

The authors have tested in mice the action of an antivenene against *L. mactans*, the Black Widow spider, obtained from the Argentine, first against *L. indistinctus* venom, and they found that 1 cc. of anti-*mactans* serum would protect the mice against 1,200 m.l.d. of the *indistinctus* venom (0·25 cc. of 1 in 60 dilution of the antiserum gave complete protection against 5 m.l.d. of the *indistinctus* venom). Next, the protective action of the same antivenene, injected intravenously in a dose of 0·2 cc. of a 1 : 5 dilution, was tested when given 25 hours after intramuscular injection of *indistinctus* venom. All the mice survived, but two controls died in 28 and 32 hours, respectively. Lastly, protection against the bite of *L. indistinctus* was tested, 0·25 cc. of 1 : 20 dilution of the anti-*mactans* serum being injected immediately after the bite. All the mice lived, whereas a control died in 17 minutes. Whether the action is reciprocal, *i.e.* whether *L. indistinctus* antivenene will protect against the effects of *L. mactans* bite, has yet to be proved, and until this is done it cannot be affirmed that the venoms of *L. indistinctus* and *L. mactans* are identical.

H. Harold Scott.

Bell, J. E., Jr. & Boone, J. A. **Neostigmine Methylsulfate an apparent Specific for Arachnidism (Black Widow Spider Bite).** *J. Amer. Med. Ass.* 1945, Dec. 8, v. 129, No. 15, 1016–17.

"1. In a typical case of arachnidism, the symptoms failed to respond to calcium gluconate and sedatives for a period of five and one-half hours.

"2. Dramatic and complete relief of muscle spasm and pain followed within one hour the intramuscular injection of 2 cc. of 1 : 2,000 neostigmine methylsulfate with 1/150 grain of atropine sulfate.

"3. This single case is presented in the hope that this apparently specific therapy will be tried in other cases without delay."

DERMATOLOGY AND FUNGUS DISEASES.

Wolfe, W. D. **Diseases of the Skin among the Natives of Northeast New Guinea.** *Arch. Dermat. & Syph.* 1945, Oct., v. 52, No. 4, 247–8.

"1. The dermatologic abnormalities in a group of 1,047 natives of northeast New Guinea are tabulated and discussed briefly.

"2. The most frequently encountered cutaneous diseases were scabies, ulcers and tinea ; these comprised 80 per cent. of all diseases of the skin noted.

"3. With the exception of yaws, tinea imbricata, filariasis and keratoma plantare sulcatum, the type of cutaneous disease found among the natives differs little from that seen in the United States."

Marple, C. D. **Progressive (Disseminated) Coccidioidomycosis : Report of a Case.** *Ann. Intern. Med.* 1945, Aug., v. 23, No. 2, 240–49.

HEAT STROKE AND ALLIED CONDITIONS.

Saphir, W. **Chronic Hypochloremia simulating Psychoneurosis.** *J. Amer. Med. Ass.* 1945, Oct. 13, v. 129, No. 7, 510–12.

Ten cases are described with ill-defined intestinal and nervous symptoms resembling those of psychoneurosis. The blood in all ten cases was found to be deficient in chloride, *i.e.* it contained less than 400 mgm. per 100 cc. (68·4 m : eq/L). The patients rapidly improved when given a regular diet with vitamin supplements and extra salt, and the blood chlorides rose to the normal level. The author considers that all these men were suffering from chronic hypochloraemia [although some of the improvement may well have been due to the vitamin supplements and rest]. The patients had been in the tropics for periods varying from 3 weeks to nearly 31 months [it is not stated whether they had lost weight in this time]. The author suggests that these men had not taken enough salt "to prevent a gradually increasing chloride deficit" though they had taken enough to prevent heat exhaustion consequent upon a sudden call on body salt ; and he draws attention to the possibility that chronic hypochloraemia may be missed if it is not specifically looked for.

W. S. S. Ladell.

Spector, H. & Hamilton, T. S. **The Microdetermination of Iodine in Biological Materials with special reference to the Combustion of Samples in the Parr Oxygen Bomb.** *J. Biol. Chem.* 1945, Nov., v. 161, No. 1, 127–35. [11 refs.]

Spector, H., Mitchell, H. H. & Hamilton, T. S. **The Effect of Environmental Temperature and Potassium Iodide Supplementation on the Excretion of Iodine by Normal Human Subjects.** *J. Biol. Chem.* 1945, Nov., v. 161, No. 1, 137–43.

TROPICAL ULCER.

Panja, G. **Aetiology and Treatment of Ulcus tropicum.** *Indian J. Med. Res.* 1945, May, v. 33, No. 1, 11–16, 6 figs. on 2 pls. [28 refs.]

In the latter half of 1943 numbers of cases of *ulcus tropicum* were seen in Calcutta, Orissa, Nagpur and Santhal Perganas, whereas prior to that the disease was rarely met with in Bengal. The facts that in nearly all cases the lower part of the leg was involved and the patients were Indians of the poorer classes and accustomed to go barefoot, pointed to soil infection. Healing did not produce immunity ; fresh sores might appear while others were healing or had just healed. Also the fact that the poorly nourished were the chief sufferers suggested an avitaminosis at the base of the condition, but the ulcers do not respond to diet rich in vitamins (though this deficiency may predispose), the patients presented none of the usual signs of vitamin deficiency, and one member only of a family might be affected though all had the same diet.

Fusiform bacilli were present in all and the ulcers could be produced experimentally by inoculation of the bacilli. (If streptococci were inoculated at the same time the resulting ulcer was larger and took longer to heal.) Pus from an ulcer discharging fusiform bacilli, if applied to ulcers of another kind, leprous, for example, would result in a typical *ulcus tropicum*. Filtrates of the pus from a tropical ulcer, through an L3 candle, were not infective. Inoculation of the third or fourth anaerobic subculture of the fusiform organisms produced typical ulcers in four volunteers. Treatment consisted in frequent irrigation and removal of the adherent pus, thus exposing the surface of the ulcer to the air and removing the anaerobiosis in which the organism flourishes, and applying a paint of copper sulphate ʒii, phenol ʒi, glycerine ʒi ; then irrigating to remove excess of the copper salt and ease the pain, and covering with a pad of absorbent material soaked in 1 : 5,000 potassium permanganate. Other local applications such as acriflavin, picric acid, hydrarg. perchlor. (1 : 1,000) proved of little value in the author's cases ; sulphonamides were very disappointing and vaccines of the fusiform bacilli were of no benefit.

H. Harold Scott.

Moreau, P. & Ouary, G. Premières observations de traitement des ulcères phagédéniques par la pénicilline. [**The Treatment of Tropical Ulcer with Penicillin.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 7/8, 216–35.

Clinical notes are given of 19 cases of tropical ulcer which were treated by local application of a solution of a sodium salt of penicillin. The ulcers varied in size and some required skin-grafting later, but in all the cases penicillin diminished and even abolished sepsis within a few days, and healing was usually complete within a few weeks. The applications are said to have been painless.

The salt of penicillin was in the dry state in ampoules, each containing 100,000 Oxford units ; a stock solution of 15,000 units per cc. in normal saline

was prepared and kept in the ice-chest but had to be used within 48 hours. Immediately before use it was diluted with normal saline to contain 250 units per cc.

The ulcer was first cleaned with cotton wool swabs soaked in normal saline, then its surface was rubbed with swabs soaked in penicillin solution and the ulcer was dressed with a gauze compress soaked in the solution ; the dressing was changed daily.

The advantages of the method are : ambulant treatment is possible ; absence of reaction or pain ; its simplicity. The disadvantages are : the need to keep the ampoules in the ice-chest ; the need to use the penicillin within a prescribed time limit ; the cost (18 dollars for 100,000 units).

J. F. Corson.

MISCELLANEOUS DISEASES.

HADDAD, N. N. **Muco-Cutaneous Fever.** *J. Canadian Med. Services.* Hamilton. 1945, Sept., v. 2, No. 6, 657–62, 3 figs.

This disease has been given various other names—Behcet's syndrome [this *Bulletin*, 1944, v. 41, 780 ; 1946, v. 43, 157], erythema multiforme, Stevens-Johnson's disease, ulcero-membranous stomatitis, cyclical mucosal ulceration, ulcerative stomatitis, etc. During the past 12 months, 1944–5, six cases have been treated at Fort Osborne Military Hospital, Winnipeg, Manitoba, and three of them are described in the present paper.

Case 1.—A soldier, aged 28, was admitted suffering from headache and soreness of the eyes, mouth and throat ; his temperature was 102°F., pulse 110. He had conjunctivitis, numerous ulcers in the mouth, and scattered skin lesions —all stages from macules to pustules—on the trunk and arms ; there were no genital lesions. Physical and laboratory examinations showed no indications of other disease. Local treatment, blood infusions and vitamin therapy were followed by rapid improvement and he was discharged from hospital after about 10 days.

Case 2.—A recruit, aged 19, was admitted complaining of a cold in the head and a sore mouth of 3 days' duration. He had numerous pea-sized vesicles on the lips and in the mouth and also on the glans penis ; he had slight conjunctivitis. On the next day a scattered maculo-papular eruption with lesions up to 1·5 cm. in diameter appeared on the trunk and limbs. Staphylococci were found in smears from the conjunctival and mouth lesions, and the latter also showed streptococci ; these organisms were grown in culture. During the first week his temperature was about 99°–103°F. and the stomatitis grew worse. Two days after admission he began to cough up bloody mucus and X-rays showed infiltration at the bases, especially the right base. Cyanosis and dyspnoea developed, his condition becoming serious. Oxygen was given and 200,000 units of penicillin intramuscularly, with a second dose of 300,000 units three days later. He gradually improved, becoming afebrile about 14 days after admission, and was discharged on the 42nd day.

Case 3.—A soldier, aged 30, was admitted with a few discrete ulcers on the buccal mucous membrane, and an irregular pink macular rash on the extremities with lesions 1–2 cm. in diameter. He felt and looked quite well. The lesions disappeared in about 10 days.

He was readmitted about 6 weeks later with headache, sore throat and mouth of 5 days' duration. He had slight conjunctivitis and numerous vesicles on the lips and oral and nasal mucosa ; there were also scattered

macules and vesicles on the trunk and limbs and a few similar lesions on the external genital organs. His temperature was about 102°–103°F. for a few days but soon subsided, and he recovered in rather over one week.

The authors regard the lesions of the mucous membranes as the most important part of the disease, causing the fever and the severe local discomfort.

J. F. Corson.

MOHANTY, J. K. **The Presence of Rhinoscleroma in Koraput District of Southern Orissa.** *Indian Med. Gaz.* 1945, Sept., v. 80, No. 9, 458–9.

Report of one case.

GREIG, E. D. W. **On Tropical Eosinophilia associated with Pulmonary Signs (Loeffler's Syndrome).** *J. Trop. Med. & Hyg.* 1945, Dec.–1946, Jan., v. 48, No. 6, 149–51. [27 refs.]

HAWKING, F. **The Choice of Sulphonamides.** *Practitioner.* 1946, Jan., v. 156, No. 931, 72–3. [Summary appears also in *Bulletin of Hygiene.*]

In this short note Hawking includes a table which, because it summarizes so clearly the sulphonamides suitable for the treatment of certain diseases, will be valuable to readers of this *Bulletin.* It is a condensation of the information contained in the Medical Research Council War Memorandum on the Medical Use of the Sulphonamides [see this *Bulletin*, 1945, v. 42, 1052].

Table showing which sulphonamide to use in different conditions.

Condition	Sulphonamide
Haemolytic streptococcal infections (moderately severe)	Sulphanilamide.
Haemolytic streptococcal infections (severe)	Sulphathiazole, sulphadiazine or sulphamezathine.
Otitis media	,, ,, ,,
Meningococcal meningitis	,, ,, ,,
Purulent meningitis	,, ,, ,,
Pneumonia	,, ,, ,,
Staphylococcal infections (if penicillin is not available)	,, ,, ,,
Chancroid	,, ,, ,,
Lymphogranuloma inguinale	,, ,, ,,
Peritonitis (for insertion after operation)	,, ,, ,,
Gonorrhoea (if penicillin is not available)	,, ,, ,,
Urinary infections	Sulphathiazole or sulphamezathine.
Wounds and burns (local applications)	Sulphathiazole, sulphanilamide or mixture of the two.
Bacillary dysentery	Succinylsulphathiazole, sulphaguanidine or sulphadiazine.
Prophylaxis against meningococcal infections or rheumatic fever	Sulphadiazine, sulphamezathine or sulphanilamide.

Charles Wilcocks.

DAVALOS, A. **The Rarity of Stones in the Urinary Tract in the Wet Tropics.** *J. Urology.* 1945, Aug., v. 54, No. 2, 182–4. [16 refs.]

The observations recorded in this paper were made in some of the tropical regions of Ecuador, South America. In certain areas of that country, particularly on the west coast and in the south, urinary lithiasis is of very rare occurrence; during a year of urological practice in the southern part of Ecuador the author did not see a single case among 60,000 persons examined.

The diet of the people of tropical Ecuador is poorly balanced and deficient in protein and vitamins, especially vitamin A; the large quantity of bananas eaten produces high acidity of the urine. In northern Peru, where urinary lithiasis is common, the diet is similar but the climate there is warm and dry throughout the year while in Ecuador it is hot and humid.

The average *p*H of the urine of 500 patients was 5·0; cultures of their urine were all negative for the common urea-splitting organisms (*Proteus vulgaris* and others).

The author concludes that the rarity of urinary lithiasis in certain parts of Ecuador is attributable to the fact that the profuse perspiration caused by the climate reduces the eliminatory strain on the kidneys, and the low urinary *p*H, by inhibiting the growth of urea-splitting organisms, prevents the precipitation of phosphates and carbonates in the urinary tract. The rare cases of lithiasis found are due to uric acid or cystine. *J. F. Corson.*

LEITNER, A. J. Le cancer en Côte française des Somalis. [**Cancer in French Somaliland.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 7/8, 235–41.

The author gives a tabular list of malignant growths observed radioscopically and at post-mortem examination, in natives of French Somaliland, during the years 1939–43. The total number was 24 and included primary cancer of the liver (8), cancer of the pancreas (1), cancer of the rectum (1), cancer of the stomach (2), cancer of the oesophagus (1), cancer of the tongue (3), cancer of the breast (1), epithelioma of the ear, nose, jaw, skin of the shoulder, and skin of the abdomen, one each, a mixed tumour of the parotid, and a connective tissue tumour of the thigh. Short notes of four cases of primary cancer of the liver are given and a few cases of various malignant growths in non-natives are mentioned. *J. F. Corson.*

GENERAL PROTOZOOLOGY.

NERY GUIMARÃES, F. Toxoplasmose humana. Meningoencefalomielite toxoplasmica: ocorrência em adulto e em recemnascido. [**Human Toxoplasmosis. Toxoplasmic Meningoencephalomyelitis in an Adult and an Infant.**] *Mem. Inst. Oswaldo Cruz.* 1943, June, v. 38, No. 3, 257–320, 2 pls. (1 coloured), 1 map, 28 figs. & 2 graphs. [65 refs.] English summary.

This is a long paper largely taken up with a historical summary of our knowledge of toxoplasmosis up to 1942. It is based on two cases seen in Brazil, the one in a young man, 18 years of age, and the other in an infant 14 months old. Both cases were fatal, and it was possible in the case of the adult to carry out a detailed histopathological study. This revealed a meningoencephalomyelitis characterized by extensive inflammatory areas with or without necrosis in the white and grey matter of the brain. Scattered through the tissues were miliary and submiliary granulomata, usually situated in relation

to blood vessels. Inflammatory areas were seen in the myocardium, while necrotic foci occurred in the liver and hypophysis. Typical parasites were seen in smears and in sections. They were intracellular, in pseudocysts or free.

The disease in the infant was characterized by hydrocephalus, with areas of intracerebral calcification, associated with tremors and convulsions. Diagnosis was established by the infection produced in animals by inoculation of cerebrospinal fluid.

The paper is illustrated by a number of microphotographs and a coloured plate showing the character of the parasite isolated. *C. M. Wenyon.*

Brug, S. L. & Vos, J. J. T. **Toxoplasmosis hominis.** Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1942, Nov. 28, v. 86, No. 48, 2956–63, 47 figs. on 1 pl. English summary.

"Review of the most recent literature on human toxoplasmosis. Further anatomical and parasitological details on the case observed in Groningen. In this case the sections of the brain contain parasites, which were obviously multiplying by schizogony."

i. Watson, J. M. **The Identity of the Ciliate** *Balantidium minutum*, **an Alleged Parasite of Man.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Oct., v. 39, No. 2, 151–60, 4 figs. [20 refs.]

ii. ——. **Observations on the Coprophilic Habits of a Ciliate** *Balantiophorus minutus* **Schewiakoff.** *Ibid.* 161–5. [12 refs.]

i. In the first paper the author reviews the records of the discovery of *Balantidium minutum* in human faeces since Schaudinn first described it as a human parasite in 1899. Several writers have held that the ciliate was probably not a parasite, but a coprozoic organism which is liable to contaminate stools, and that its presence has led to erroneous conclusions regarding its parasitism. The author has made a careful study of the various descriptions of the ciliate and has come to the conclusion that it is *Balantiophorus minutus* Schewiakoff, a free-living ciliate which, under certain conditions, may live and multiply enormously in human faeces after they have left the body.

ii. In the second paper are given the results of an investigation into the factors which favour or inhibit the development of *Balantiophorus minutus* in human faeces. In normal stools active multiplication may occur, leading to fantastic abundance of the ciliates. In abnormal stools from various sources, whether loose, diarrhoeic or dysenteric, there was usually not only a failure to develop, but rapid extinction occurred. The reasons for this were found to be the presence of urine, bile salts or traces of drugs, and conditions of high osmotic pressure. It was determined by experiments on mice that cysts of the ciliate were unable to survive passage through the intestine. Faeces of mice fed on cysts, when emulsified in water, failed to yield cultures of the ciliate, which, however, developed vigorously when inoculated directly into such faecal emulsions. *Balantiophorus minutus* is a soil protozoon and as such is capable of living in an amoeboid form in mere surface films of water and is capable of surviving a considerable degree of drying in the unencysted state. These qualities enable it to live and survive in the viscous semi-solid material of a stool in which any ordinary ciliate would rapidly succumb. This does not mean that an organism of this type is capable of living in the human intestine. In fact, it has never been proved that any free-living protozoon can enter the intestine of a warm-blooded animal in the encysted stage and emerge from the cyst to survive or multiply in some part of the intestine. In the supposed

infections with *Balantidium minutum* it seems clear that the stools, after being passed, became contaminated with airborne cysts or water-borne free-living forms of *Balantiophorus minutus*. *C. M. Wenyon.*

GENERAL ENTOMOLOGY.

BATES, M. **Observations on Climate and Seasonal Distribution of Mosquitoes in Eastern Colombia.** *J. Animal Ecology.* 1945, May, v. 14, No. 1, 17–25, 1 pl. & 3 figs. [13 refs.]

This area of Eastern Colombia (S. America) has a remarkably uniform climate, with only 2·8°C. difference between the mean temperature of the hottest month (February, 27·8°C.) and of the coolest (July, 25·0°C.). There is a greater variability in rainfall, though even in the driest month (February) there is usually more than 3 in. (87 mm.) of rain. May is the wettest month with 28 in. (690 mm.); the annual precipitation is 180 in. (4,645 mm.). Even in the driest month the noon relative humidity does not fall below 60 per cent.

Most attention in this investigation was paid to *Haemagogus capricorni*, a probably important vector of jungle yellow fever, but other species of mosquitoes were also studied. Diurnal captures were made by men standing in various locations and catching all mosquitoes that came to bite. Nocturnal species were caught in a " stable trap " baited with a donkey.

Haemagogus capricorni was by far the commonest diurnal mosquito, accounting for nearly 80 per cent. of those captured. *Anopheles rangeli* comprised over 50 per cent. of the nocturnal catch.

Most species were scarcest in March, *i.e.* at the end of the " dry " season. They then reached a maximum about June, and fluctuated for the remainder of the year. The reasons for these fluctuations are discussed.

Kenneth Mellanby.

ROUBAUD, E. & COLAS-BELCOUR, J. Influence de la salure des eaux sur le développement de l'*Aëdes aegypti*. [**Influence of Salinity of Water on the Development of** *Aëdes aegypti*.] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 5/6, 136–45. [12 refs.]

In a large series of experiments, gravid female *Aëdes aegypti* were given water of five different salinities, ranging from tap water (containing only 0·146 gm. NaCl per litre) to full strength sea water, in which to oviposit. The 17,940 eggs laid in all these experiments were distributed as follows: tap water, 28·9 per cent. of the total eggs; tap water plus 31 per cent. sea water, 28 per cent.; tap water plus 42·6 per cent. sea water, 22 per cent.; tap water plus 62 per cent. sea water, 17·8 per cent.; sea water, 3·1 per cent.

Observations on the activities of the insects revealed that non-gravid and gravid females alike (and also males), were equally attracted to all these five samples of water. Egg laying is soon discontinued in the strong saline solutions, the saline concentrations being apparently detected by the posterior extremity of the abdomen which comes into contact with the water-surface during oviposition. *Kenneth Mellanby.*

BELKIN, J. N. *Anopheles nataliae*, **a New Species from Guadalcanal.** *J. Parasitology.* 1945, Oct., v. 31, No. 5, 315–18, 6 figs. on 1 pl.

KENNEY, M. **Experimental Intestinal Myiasis in Man.** *Proc. Soc. Exper. Biol. & Med.* 1945, Nov., v. 60, No. 2, 235–7.

"From 60 volunteers fed with living maggots of *Musca domestica*, Calliphora, and Sarcophaga, under conditions to avoid their destruction in the stomach, only 10 failed to have symptoms of gastro-intestinal disturbance.

"In 50 cases men had nausea, vomiting, intestinal cramps and diarrhea together or as separate symptoms, but all symptoms disappeared within 48 hours following the elimination of the larvae, of which only a few were found alive in the vomitus and stools.

"These findings seem to indicate that though temporary gastro-intestinal distress may follow the ingestion of such dipterous larvae as *Musca domestica*, Calliphora, and Sarcophaga, they do not produce a true intestinal myiasis in man."

BEAMENT, J. W. L. **The Cuticular Lipoids of Insects.** *J. Exper. Biol.* 1945, Aug., v. 21, Nos. 3 & 4, 115–31, 7 figs. [31 refs.]

POWNING, R. F. **The Analysis of D.D.T. and Pyrethrins in Kerosene-based Sprays.** Reprinted from *J. Council Scient. & Indust. Res.* 1945, May, v. 18, No. 2, 121–3.

A method developed for the separation and analysis of DDT and pyrethrins n a mixed insecticide spray is described. *J. R. Busvine.*

LABORATORY METHODS.

HAY, S. **Despatch of Material for Histological Examination.** *Edinburgh Med. J.* 1945, Nov., v. 52, No. 11, 426–9.

Correct treatment of tissue before posting it to a laboratory for histological examination is specially important in the case of biopsy tissue. The three main injunctions are: (1) put it at once into fixative without previous washing in water; (2) do not cut into it; (3) send it without delay. The best general fixative is a mixture of formalin with 9 parts of tap water.

Biopsy material may be: (1) large, such as a breast with the glands; (2) medium-sized, such as an encapsuled tumour, and (3) small, such as uterine curettings. In the case of large material, if the surgeon wishes to see the type of lesion, he should not gash it irregularly but should make one planned cut in the most suitable axis, not quite through the whole but so as to leave a hinge so that the whole can be closed up again. Medium-sized material should be at least $\frac{1}{4}$ to $\frac{1}{2}$ in. thick and should be cut in the best direction to include all tissues, affected and healthy, including an advancing margin and a diagnostic part. If the specimen is too large for despatch in fluid, it may be wrapped in formalin-soaked cloth covered by "Cellophane" or gutta-percha tissue. Small material such as uterine curettings should be put into a small linen bag (not a gauze bag) in the fixative to avoid any loss.

In all cases, freshly removed tissue should never be placed on dry gauze as this has a powerful desiccating capillary effect.

Bottles should be nearly full as a large volume of air tends to injure the specimens. They should, of course be securely sealed and packed, and notes should be enclosed. *J. F. Corson.*

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